USER'S MANUAL

AMP
NONINVASIVE SCREENING HEMOGRAM ANALYSER

Manufacturer: BIOPROMIN Ltd.,
Residence: UKRAINE

ALTA.941320.001

30 May, 2009

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Attention! Before use of the system you have to read carefully the USER'S MANUAL to understand function of the system!

1. Description of the AMP non-invasive screening hemogram analyzer and its function

1.1 Purpose of the AMP non-invasive screening analyzer

The AMP non-invasive screening hemogram analyzer is medical device which actually is able to define HGB, HCT, RBC, WBC, Lymphocytes (LYM), PLT, Na^+, K^+, Ca, total protein (TP), cholesterol (CHOL) upon measuring the temperature at certain biologically active points of human body surface using the non-invasive method. **The system has continuously been developed. Measuring techniques and the software development will allow further parameters measurement with accuracy more than the required existing ones.**

Results of the non-invasive examination are preliminary, giving highlights to more accurate and detailed in vitro examinations results.

1.2 Basic principle of AMP device function

Function of the AMP analyzer is based on interrelation of work of the blood circulation system of insides with heat of chemical reaction of Nitrogen, Oxygen, Hydrogen and Carbon. Changes of temperature determine the activity of chemical elements through interrelation of Nitrogen compounds and Hydrogen bound-

ing furthermore, through interrelation of Oxygen melting factor changes.

The goal of the examinations is determination of changes in composition of blood shaped elements and during the end of chemical reactions which have interconnects with Oxygen consumption and Carbon dioxide exhaust regulated by organism, having influence to level of protein and lipids in cell membranes.

Taking into consideration, that the AMP non-invasive screening hemogram analyzer measures the temperature through optic sensors, there is no any influence to the patients' organism.

1.3 Function of the AMP non-invasive screening analyzer

Principle of function of the AMP non-invasive screening hemogram analyzer is based on measurement of temperature of biologically active "reference" point of the human body which data loaded, to PC from keyboard is then processed there.

Device has five sensors, which are to be placed onto so-called biologically active points of patients' body.

Bioactive or so-called reference-points used during examination, are following:

- Bifurcation of the right and left neck artery (two points)
- Right and left armpit (two points)
- Umblical area (one point)

Prior to examination, the five sensors are to be placed onto patient, and the personal data of him, and breath rate, pulse rate are to be loaded to PC from the keyboard. Then the data collection and calculation-software starts.

Non-invasive screening hemogram analyzer processes signals coming from sensors placed on body of the patient, converts these signals to digital form and passes them to the PC.

The PC makes processing of the measured data by means of appropriate software, and, after the necessary running time makes the measured data visible on the display. Result of examination can be printed out in form of medical report.

Non-invasive screening hemogram analyzer works in time multiplex mode with repeating data collection.

Data sending speed to PC is 56700 bit/s.

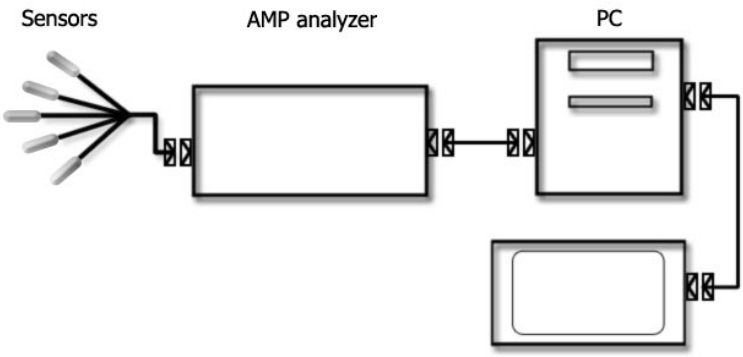
Quantity of the measuring data stored in memory is not less than 64000.

Calculation of the data of blood test parameters is made by special examination algorithm named Malykhin-Pulavskyi method (Ukrainian Patent Nr. 3546 A61B5).

1.4 The intended field of application of the analyzer

Intended field of the application of the device: clinics, medical research centres, sanatoriums and other medical institutions to provide preliminary finding examination.

Schematic diagram of the device is shown on drawing 1.



Drawing 1. Schematic diagram of the AMP system

Non-invasive screening hemogram analyzer is sealed by two seals placed on fixing bolts under the case of device and near connectors.

1.5. Risks of the use of AMP non-invasive screening hemogram analyzer and limits of examination method

Examination cannot be executed in the following cases:

- patient has a fever;
- there are inflammations or purulent places on the body of patient close to the biological points (where sensors are to be placed), or lymphatitis;
- there are scartissues on any of the bioactive surface;
- there are fresh recovering wounds after surgery or so on any of the bioactive surfaces;

- in case the patient is in state of psychomotor agitatio;
- the sensors were not cleaned carefully by alcohol before placing them onto the bioactive surfaces;
- temperature in the examination room does not exceed range of 18 – 32 °c;
- in case the sensors do not work properly: no any sensor is allowed to indicate temperature beyond range of 27 – 38 °c;
- in case the atmospheric pressure goes beyond range of 97,3 – 105,3 kpa (730 – 790 hgmm);
- in case if the humidity raises over 80 %;
- in case if near the analyzer there is other device generating electromagnetic field with frequency below 26 hz or over 1000 mhz.

2. Technical data of the AMP non-invasive screening hemogram analyzer and characteristics of the system

2.1 Technical data of the analyzer

PC mains voltage:	230 V ± 10 %; 50/60 Hz
Analyzer mains voltage:	from USB port
U = 5 ± 1 V DC	I = 95 mA
Consumption:	max. 0,475 VA
Dimensions (WxDxH):	160mm x 100mm x 45mm
Weight: (w/cables&sensors)	0,35 kg
IP Class:	II
Protection of patient:	BF

EMC: in accordance with EN60601-1-2-2002

IP Class of Analyzer: IP 20

Readiness time counted from switching on: max. 3 min

Time of examination: 730 s

Quantity of sensors connected to Analyzer: 5

Range of temperature of reference points: 24 – 42 °C

Margin of error of reference points: max. ± 0,75 °C

Length of cables for sensors: min. 1,5 m

Connection of Analyze to PC: PS bus

Method of diagnostic: Malykhin-Pulavskyi (data collection from reference point)

After switching on Analyzer runs self-test program, to inspect readiness of the software.

By implementation of the users' software, Analyzer can be set to different modes.

2.2 Functions of the Analyzers' software:

- Loading of the patients' demographic data and physiological data to the memory of the Analyzer;
- Data collection from sensors and data processing;
- Data view on the screen;
- Saving the data to database;
- Printing out of the results;

2.3 Minimum requirements of the PC hardware:

Processor:	Pentium, or equivalent
RAM:	min. 32 Mb (85 ns)
HDD:	4,3 GB (17 ms)
CD-ROM	
Display:	SVGA 14"…17" definition 1024x768 pixels

2.4 Ambient conditions

Working ambient temperature:	10 – 35 °C
Atmospheric pressure:	101,3 ± 4 kPa
Humidity	max. 80 % (+25 °C) (non-condensing)
IP Class:	II
IP Class at side of patient:	BF
EMC:	in accordance with EN60601-1-2-2002
Analyzer IP Class:	IP 20
Amb. temp. of transportation:	-50 °C – +50 °C
Measuring time range:	180, 360, 720 s

2.5 Data of patient loaded prior to examination

Data to be loaded by keyboard prior to examination:

Name and Surname of patient

Age of patient

Weight of patient

Pulse frequency of patient

Breath frequency of patient

2.6 Examination data:

Blood of patient:

- haemoglobin concentration (HGB) [mg/l or mmol/l]
- haematokryte (HCT) [l/l]
- red blood cell (RBC) [10^{12}/l = T/l]
- white blood cell (WBC) [10^{9}/l = G/l]
- lymphocyte quantity (LYM) [%]
- thrombocyte quantity (PLT) [10^{9}/l = G/l]
- serum Na^{+} concentration [mmol/l]
- serum K^{+} concentration [mmol/l]
- serum Ca concentration [mmol/l]
- cholesterol concentration (CHOL) [mmol/l]
- total protein concentration (TP) [g/l]

2.7 Accuracy of the data of examination:

HGB	120-180 [mg/l] ±10 %;	60-120 and 180-300 [mg/l] ±15 %;
HCT	0,37-0,52 [l/l] ±10 %;	0,16-0,37 and 0,52-0,65 [l/l] ±15 %;
RBC	3,8-6,2 [T/l] ±10 %;	2,6-3,8 and 6,2-7,6 [T/l] ±15 %;
WBC	5-9 [G/l] ±10 %;	3-5 and 9-25 [G/l] ±15 %;
Lym %	20-35 [%] ±10 %;	15-20 and 35-50 [%] ± 15 %;
PLT	140-450 [G/l] ±10 %;	80-140 and 450-600 [G/l] ±15%;
Na^+	133-147 [mmol/l] ±10 %;	beyond normal range ±15 %;
K^+	3,4-4,5 [mmol/l] ±10 %;	beyond normal range ±15 %;
Ca	2,25-2,65 [mmol/l] ±10 %;	beyond normal range ±15 %;
Cholesterol	2,50-7,80 [mmol/l] ±10 %;	beyond normal range ±15 %;
Total protein	60-80 [g/l] ±10 %;	beyond normal range ±15 %;

2.8 Details of the whole system

Chart Nr 1. Accessories of the whole system

Item	Mark	Q'ty
1 AMP	ALTA.941320.001	1
2 Cable w/ 5 sensors	ALTA.941320.002	2
3 Cable for connecting analyzer and PC USB bus	ALTA.941320.003	1
4 Manual	ALTA.941320.001 RE	1
5 Installation (USPIH) software on CD	ALTA.941320.004	1
6 Key Guardant Stealth II	ALTA.941320.005	1
7 Cover	ALTA.941320.006	1

3. Build-up and structure of the non-invasive screening analyzer

APM non-invasive screening hemogram analyzer and the PC connected via UBS port is seen at picture 2.

Non-invasive screening hemogram analyzer with rigid plastic case has a following main parts: processor unit at PCB, analyzer unit, interface processor connected to USB bus of PC, socket for patients' cable and cable of PC interface with USB port.

On front plate of device the patients' cable socket, LED for indication of PC and analyzer connection, and USB bus for PC connection.

Five sensors connected to analyzer measure temperature of patients' reference point with accuracy not less than $\pm$ 0,5 °C. Parameters of temperature are sent by sensors with speed 56700 bit/s to central processor

unit of the AMP non-invasive screening analyzer. Demographic and physiological data loaded from keyboard also are sent there. Data given are processed by central processor unit and are sent to PC which makes them possible to view and print.

Picture 2. AMP non-invasive screening hemogram analyzer and PC connected to it

3.1 Color coding of cables

Chart 2. Connection points of sensors and colour coding

Connection point of sensor	Colour code
Bifurcation of left artery	Blue
Bifurcation of right artery	Green
Left armpit (axillaries)	Yellow
Right armpit (axillaries)	Pink
Abdominant area (umbilicus) (paraumbilicalis)	Red

4. Control of the system

Function of the system is provided by program of the central processing unit of analyzer and software loaded to PC, in time sequences set by operator (180 s, 360 s, or 720 s). Connection of the analyzer to PC in working condition is indicated by LED on the front panel.

Software installed on PC provides indication of following modes:

- Calculation time sequence;
- Connection of non-invasive screening hemogram analyzer to PC via virtual serial port;
- Proceeding of calculation process (time sequence readiness);
- Indication of errors in software and analyzer on windows on screen with information about cause and way of elimination;

- Printing out the results of examination;
- Saving the data to database, recall and print out when necessary.

5. Software packet

”USPIH” installation software is supplied on CD with the equipment. Prior to use the analyze, it is necessary to install the software to PC. During installation new directory appears on hard drive, containing following files (C:\Program Files\USPIH):

- biolika5.exe – real time control program;
- biopromin.doc – licence agreement for software;
- USPIH_EN.chm– help;
- pacient.db, pacient.px – database files;
- confdbe.ini – database configuration file;
- qtinf.dll – function file;
- FTDI directories – PC interface drivers files;

Other files necessary for operation of interface drive.

”USPIH” software can be used with PC II and higher, running with Windows - Vista/XP/2000/2003 or equal, or higher level software.

6. Examination of non-invasive screening blood test and metabolite test and indication of calculation results

Blood test and metabolite parameters definition are to be made in following sequence:

6.1 Connect patients' cable to socket DB9 of analyzer and fix it by screws (analyzer gets mains power from PC, therefore it is out of voltage).

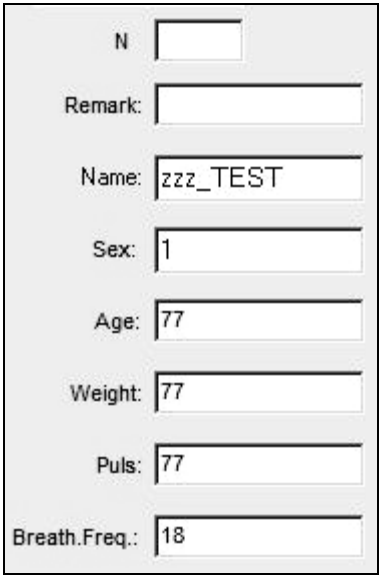
6.2 Connect USB cable supplied with PC to analyzer and USB port of PC.

6.3 Switch on the PC.

6.4 Clicking to icon on the screen run the USPIH software.

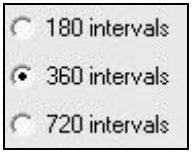
6.5 Place sensors onto patient.

6.6 Load demographic and physiologic data of patient by means of keyboard of PC in sequence shown below: (hospital class is not obligatory), Name, Surname, Sex, Weight, Pulse rate, Breath rate as it shown on picture 3.



Picture 3: Data entry of patient

6.7 Click to calculation time sequence (picture 4).

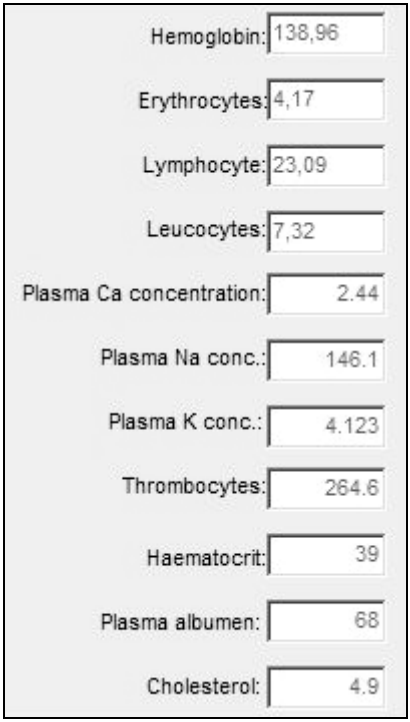


Picture 4: Calculation time sequence entry

6.8 Click by mouse at upper menu to Start or run the processing program by F9 (picture 5).

Picture 5: start of the data processing program

When processing is completed, examination data appear automatically on the screen (picture 6)



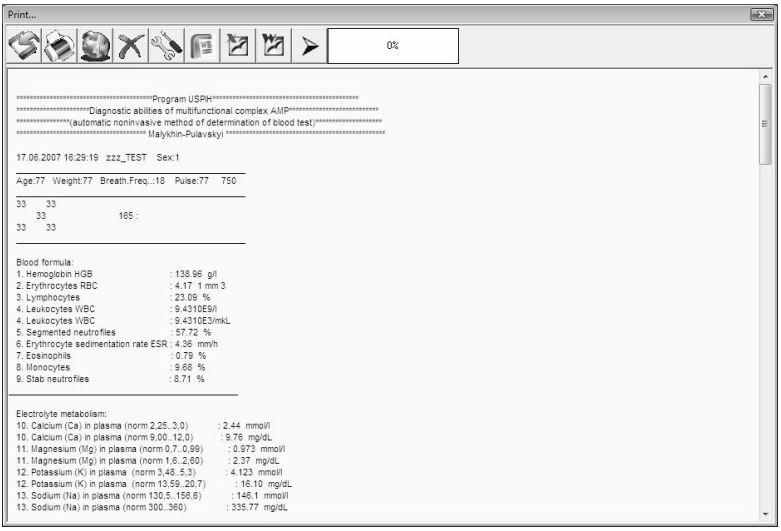
Picture 6: Examination results window

Examination data calculated by PC are saved automatically.

6.9 Remove sensors from the patients' body.

6.10 Results of examination can be printed out by "Print" menu (pictures 7 and 8).

Picture 7: Printing the examination data after preview of results on picture 8.



Picture 8: Preview of examination results on the screen.

7. Normal use of analyzer

7.1 General safety rules

It is prohibited to use the analyzer if:

- ambient temperature is higher than + 35 °C or lower than +10 °C;
- humidity is higher than 95 %;
- aggressive vapour present in the air;
- dusty spaces;
- direct sunshine;
- strong electric and magnetic fields present;
- moist environment

ATTENTION! Avoid patient and PC connecting cable against damages and do not bend when disconnecting cable from socket of analyzer. Only plug pulling out is allowed. Do not pull cable itself.

ATTENTION! During normal operation of PC it is prohibited to connect cable of analyzer to USB port or to disconnect plug from socket of USB port.

ATTENTION! Keep cable connection sequence. Connect patients' cable to analyzer first, and then connect non-invasive screening hemogram analyzer to USB port of PC.

7.2 Safety measures

Warning! During operation and maintenance of the system, the following safety measures shall to be kept:

a) It is prohibited to use the analyzer in case of damaged cable isolation.

b) Before use make a visual inspection of case of analyzer that there are no any broken or torn parts or other kind of mechanical damage.

c) Avoid the analyzer against moisture condensation. In case of fast ambient temperature change, allow at least 30 minutes to evaporate the moisture.

d) It is prohibited to connect any cable to any socket, or disconnect any cable from any socket if the PC is switched on.

e) Power cable of PC shall have protective ground wire, and the plug shall have ground connection, and shall be conform with mains socket.

f) Data processing units connected to device shall be used with safety transformer which shall meet requirements of standard MSZ:60601-1/1997 related to medical devices (e.g. ST-200 transformer made by Standel Ltd.).

g) Do not twist the mains cable, and place it the way, to avoid its damage and against jamming among other objects.

h) It is prohibited to use aerosols and liquids for cleaning the device.

i) Always place the analyzer on stable and solid surface.

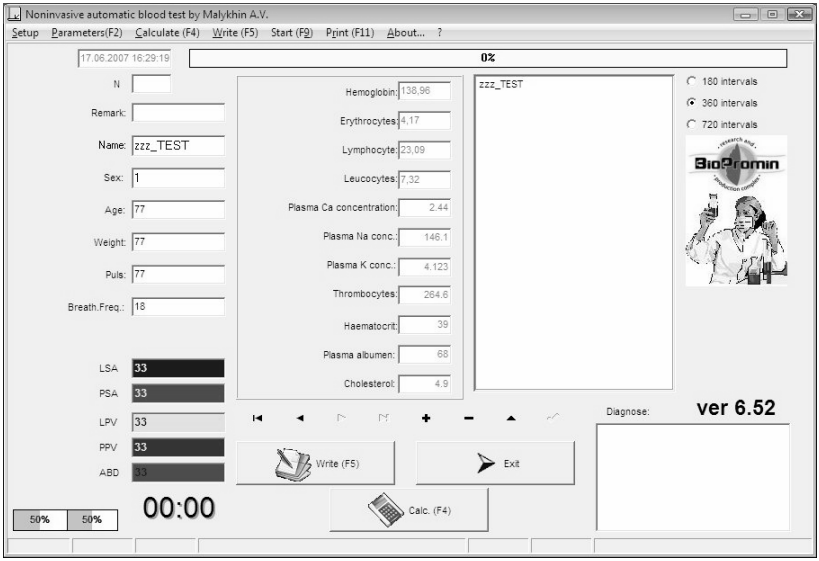
j) Always restart the PC allowing 20 minutes at least.

k) It is prohibited to use the analyzer in tinderbox, e.g. in room where flammable sleeping-draughts are kept.

8. General description of the USPIH software

Most of the operations connected with analyzing are executed by USPIH software running on PC.

USPIH software runs under WINDOWS operation system. USPIH program can be recalled by clicking by mouse at USPIH icon at desk or Start button on bottom of Windows tools, and then, select the USPIH program from “All programs” menu list. The initial window of USPIH program is shown at Picture 9.



Picture 9. Initial window of USPIH program after selection of the program

Upper tool menu at window there are the following buttons of menus (picture 10):

- Setup
- Parameters (F2)
- Calculate (F4)
- Write
- Start
- Print
- About

Picture 10. USPIH program menus

- **Setup** menu contains the followings (***factory setup***):

1. Language.
2. Report setup.
3. Print setup.

Parameters (F2) menu contains further additional parameters calculated by program and view of the preliminary report for diagnosis necessary for doctor.

- **Calculation (F4)** menu serves for preliminary calculation of blood test parameters and other biochemical data.

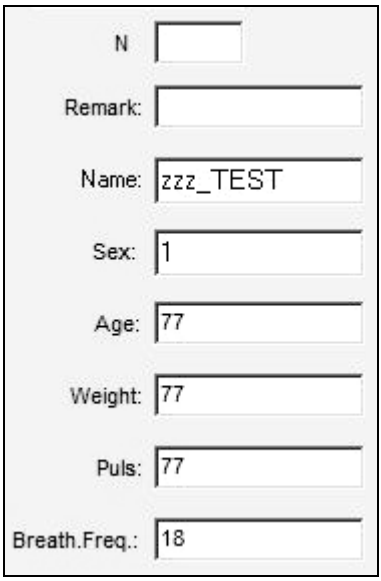
- **Write:** clicking to that button program calculates all the calculation parameters and save that to database. It is important in case of use new version of the program or for search patients' empty or wrong filled in datasheets.

- **Start** menu starts calculation of examinations results.

- **Print** menu makes possible preview of data to be printed and printing the results.

- **About** make possible searching by word in Windows.

At left side of initial window of USPIH program (picture 9) there is a field for loading demographic and physiological data of patient (picture 11).



Picture 11: field for filling in demographic and physiologic data of the patient

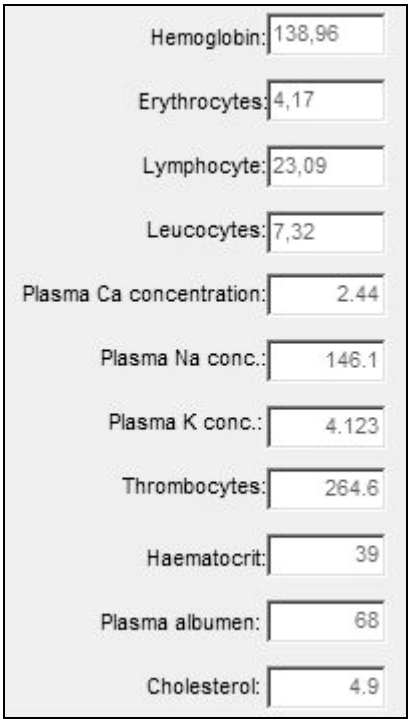
Function of rows on data loading field:

- Remark: notices connected with patient (e.g. ward, or any other);
- Name: name of patient;
- Sex: sex of patient (M-1/F-0);
- Age: age of patient;

- Weight: weight of patient;
- Pulse rate: pulse arte of patient;
- Breathing rate: breathing rate of patient;

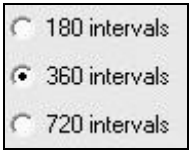
Filling in the ”Remark (*Ward filling is not obligatory)* is to be made by letters, other fields are to be filled in by numbers (Name, Sex).

At middle field of initial window of USPIH program (picture 9) there is a blood test and metabolite results data field (picture 12).



Picture 12. Field of view results of blood test and metabolite examination

Field at right of results indication field shows names of previous patients in alphabetical order, and at very right side, there is a field to indicate test time sequence (picture 13).



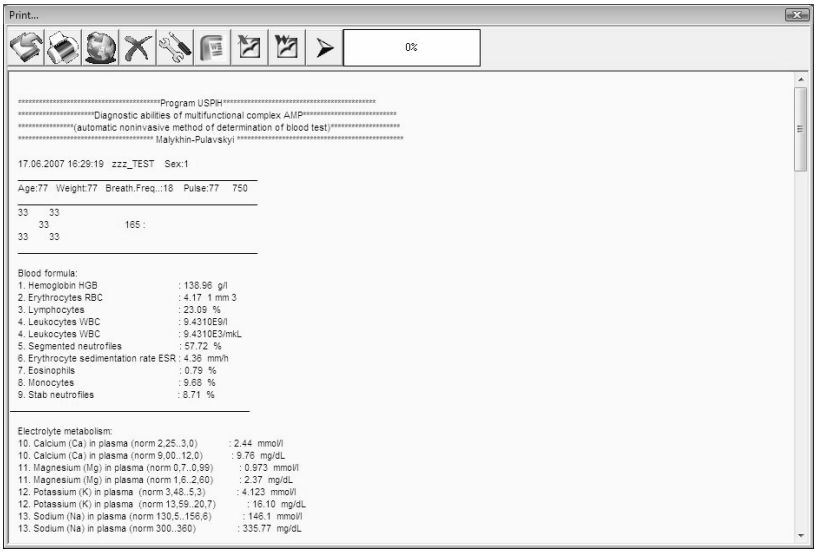
Picture 13. List of patients and time sequence

At left bottom side of the initial window of USPIH program (on picture 9) digital stopwatch is shown (picture 14) which is to be used during measurement of pulse rate of patient. Stopwatch starts by clicking to field 00:00 or pushing buttons Alt+S.

Picture 14. Stopwatch

Preview is possible by clicking to button Print on top menu of USPIH program initial window (picture 15). Picture 16 shows an example.

Picture 15. Initial window of USPIH program.



Picture 16. Print preview and print window

There are buttons at top menu of window (picture 16). They allow to:

- Save a report to a file;
- Print a report;
- Update of software
- Clean the window
- Fonts
- Export to MS Word
- Export to Open Office Calc
- Export to Open Office Write
- Exit from the window.

9. Non-invasive screening hemogram analyzer function test

Usually, function test of analyzer shall be proceeded prior to each shift, during initial switching on of the device, as follows (**tests are carried out in atmosphere pressure 750 mm of mercury column**). **Validity period for tests is 1 year**. Tests must be done only by manufacturer or representative company.

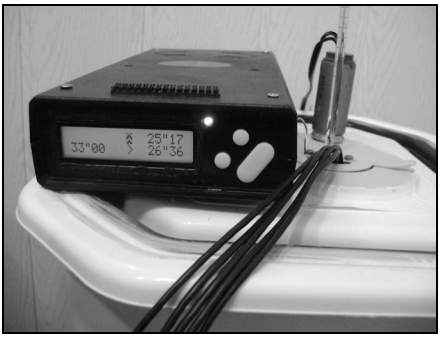
9.1 Connect patients' cable to socket DB9 of analyzer and fix it by screws.

9.2 Connect USB cable to analyzer and to PC.

9.3 Switch on the PC.

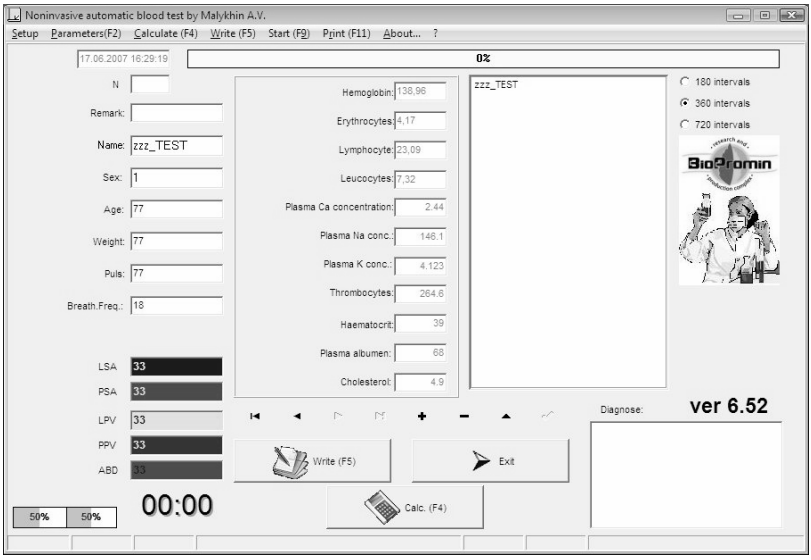
9.4 Run USPIH software by clicking to its icon.

9.5 Place sensors into vessel with glycerin at 33°C as it shown at picture 17. Check the temperature of the glycerin by common gauge.



Picture 17. Placement of the sensors during function test of analyzer.

9.6 Fill in the data fields of patient (name, sex, age, weight, pulse rate, breathing rate) as it shown at picture 18.

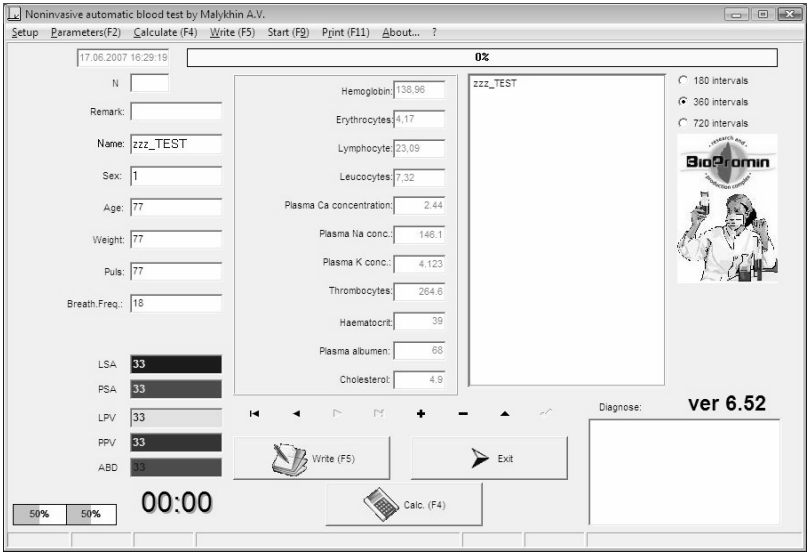


Picture 18. Data sheet of patient.

9.7 Click on Start menu at upper tool menu of USPIH program. Label of the button will change to Stop.

In field of program running progress under upper menu growing numbers will appear (0 % …100 %), and, in accordance with examination sequence (180 sec, 360 sec, 720 sec) red, green or blue bends will appear, filling up from left to right. When the time sequence ends, label Stop of menu button will change to Start label again and the program will stop calculation.

Test is successful if results are the same as it shown on picture 19, with following conditions:



Picture 19. Analyzer function test result

In fields **LSA, PSA, LPV, PPV, ABD** the same data will appear, e.g. 33. Difference between data shall not exceed ± 0,1.

Should the device not meet that requirements, it shall be considered faulty, and its use is prohibited until its repair.

10. Execution of non-invasive screening blood test and metabolite examination

10.1 Make a non-invasive screening blood test and metabolite examination as it is described in para. 6. Pay attention to place sensors in color sequence as it is described in para. 3.1.

10.2 Diagnosis, saving, data processing and activation are subject to local regulations and rules.

10.3 Remove sensors when examination is finished.

10.4 Switch off the PC.

11. Cleaning and disinfection of analyzer and its accessories

Attention! Prior to cleaning and disinfection of analyzer surface, all the cables shall be removed from non-invasive screening hemogram analyzer sockets.

Attention! Disinfection of the surface and patient cable by spirit or other, aggressive chemicals or solvents (phenol based chemicals, ester, benzyl, prop anole, chlorophorm or acetone is PROHIBITED.

Attention! Disinfection of analyzer and its accessories by heated air is PROHIBITED.

11.1 Wipe case of analyzer by soft squeezed wet cloth dipped to soap water.

11.2 Disinfection of analyzer surface is to be made by disinfectant approved by Ministry of Welfare.

Avoid analyzer against getting in the liquid inside during cleaning and disinfection of analyzer case.

11.3 Clean case of analyzer by dipped to soap water squeezed cloth.

11.4. Disinfection of cables is to be made by disinfectant approved by Ministry of Welfare.

11.5. Disinfection of sensors is to be made by 96 % purity spirit.

Do not wipe sensor by cloth as it may cause scratches on its surface.

To provide life expectancy of analyzer, cables and sensors, it is PROHIBITED:

- to bend cables of sensors and PC;
- to remove sensors from patient pulling the cables, or to pull cables from sockets;
- to wipe surface of sensors to clean them, or to use any solid, abrasive materials for cleaning.

12. Maintenance of the non-invasive screening hemogram analyzer

Maintenance of the analyzer is provided by staff of user in accordance with timetable in Chart 3.

Chart 3. Maintenance of the **non-invasive screening** analyzer

Item	Timetable		
	every-day use	after sto-riage	after trans-porta-tion
function test (chapter 10 para. 1-7)	daily	+	+
visual inspection of analyzer, connections, cables and sensors for damages	daily or if required	+	+
cleaning of analyzer (chapter 12 para. 1-2)	daily	+	+
periodic inspection by manufacturer	annually and after repair	-	-

Warranty and other repair is provided by

ONKOCET Ltd., Sreznevskeho 17, 831 03 Bratislava, SLOVAKIA

Tel/Fax: +421-2-44640977 e-mail: onkocet@gmail.com
www.onkocet.eu

Warranty repair of PC is provided by dealer.

13. Search of fault and elimination of faults

Analyzer is an accurate measuring device repair of that is to be provided by manufacturer or its local representative. Chart 4 contains possible faults requiring presence of manufacturer or its representative.

Chart 4. Search of faults and elimination of faults

Fault	Possible reason	Elimination of fault
There is a disturbing signal on one or more sensor	1. Sensors are placed not properly on body	Check up placement of sensors as it tight enough
	2. Disruption of one or more cables	Contact representative of manufacturer
No data collection during examination	Disruption of analyzer usb cable or connection fault of socket	Check up usb cable and sockets

14. Periodic inspection of non-invasive screening analyser

Periodic inspection of the non-invasive screening hemogram analyzer is to be made annually after its use or storage. Manufacturer provides inspection described below during manufacturing and annually and after repair.

Chart 5. Devices used during periodic (annual) inspection

1	Diaphragm barometer	Measuring range: 50 – 760 Hgmm
2	Aspiration humidity measuring device	Measuring range: RH = 20 – 90 % (16 – 40 °C)
3	Precision digital thermometer	Measuring range: 0 – 100 °C (error ≤ 0,036 °C)
4	Ultra thermostat with digital readout	Temperature range: 0 – 60 °C Measuring accuracy of thermostat: ± 0,15 °C

During periodic inspection of the device unpack the analyzer and keep in the room for inspection at least for 24 hours.

Execution of inspection (provided by service):

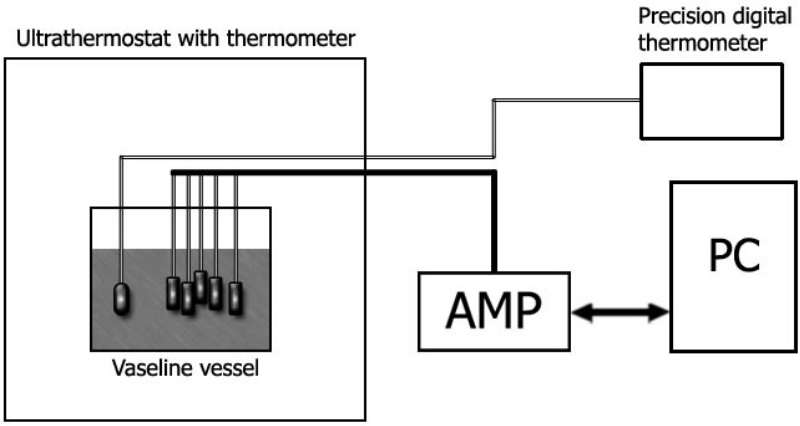
14.1 Connect patients' cable to socket DB9 of analyzer and fix it by screws.

14.2 Connect USB cable to analyzer and USB port of PC.

14.3 Switch on the PC.

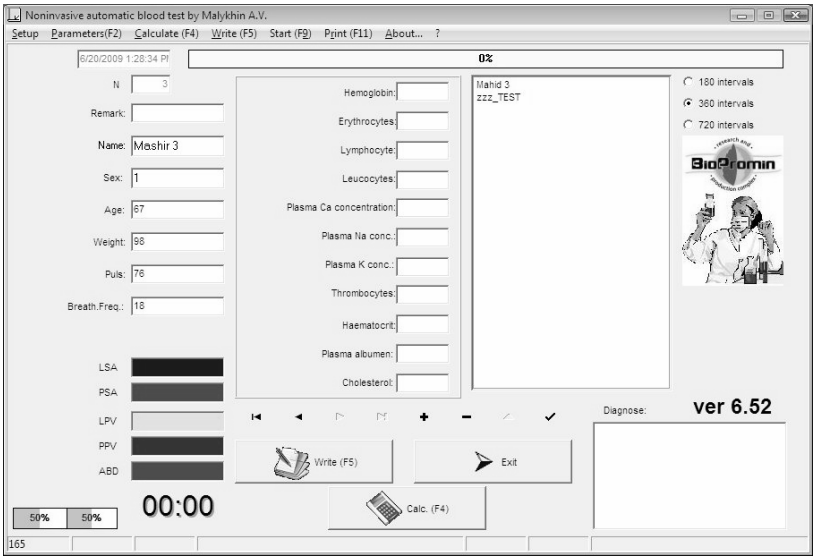
14.4 Run the USPIH software clicking to icon.

14.5 Place sensors into vessel filled by vaseline and place the vessel into thermostat. Arrangement is shown at picture 20. Set the thermostat temperature 33 °C. Wait until the temperature of the vaseline will be stabilized at level of set temperature.



Picture 20. Arrangement of periodical inspection of analyzer

14.6 Load the patients' data to fields name, sex, age, weight, pulse rate, breathing rate as it is shown on picture 21.



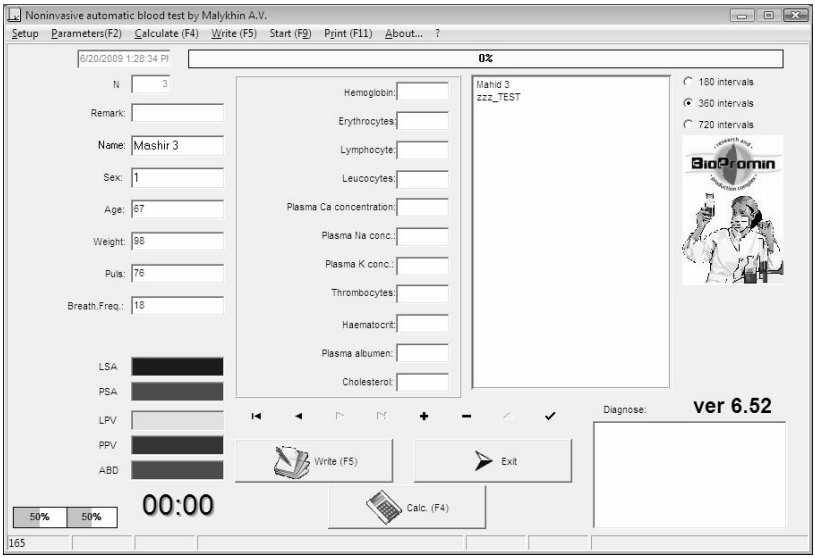
Picture 21. Loading the data to program

14.7 Click to Start menu at upper toolbar of USPIH program. Label of button will change to Stop.

14.8 In field of program running progress under upper menu growing numbers will appear (0 % …100 %), and, in accordance with examination sequence (180 s, 360 s, 720 s) red, green or blue bends will appear, filling up from left to right. When the time sequence ends, label Stop of menu button will change to Start label again and the program will stop calculation:

14.9 Test is successful if results are the same as it shown on picture 22, with following conditions

14.10 In fields **LSA, PSA, LPV, PPV, ABD** the 33 ± 0,1 data will appear.



Picture 22. Result of analyzer function test

14.11 Check up of temperature range at reference points as it is seen on picture 23 arranged as described above.

a) Set the thermostat temperature at 24 °C, check up after 30 minutes whether the temperature of the thermostat reached the set temperature (24 ± 0,5 °C) and then read out and record temperature of Vaseline indicated on precision thermometer, and temperature measured by all the sensors of the AMP non-invasive screening hemogram analyzer (1, 2, 3, 4, 5).

b) Repeat the procedure at vaseline temperatures 26 °C, 28 °C, 30 °C, 32 °C, 34 °C, 36 °C and 37 °C set by thermostat reading temperature indicated by precision digital thermometer and temperature measured by each of sensors of AMP non-invasive screening hemogram analyzer (1, 2, 3, 4, 5) (see Chart 6).

Chart 6

24 ºC			
OT	№	AMP	Δ
24,25	1	24.30	0,05
	2		
	3		
	4		
	5		

26 ºC			
OT	№	AMP	Δ
25,75	1		
	2		
	3	25.7	- 0,05
	4		
	5		

28 ºC			
OT	№	AMP	Δ
28,4	1		
	2		
	3		
	4	28.36	- 0,04
	5		

30 ºC			
OT	№	AMP	Δ
30,2	1		
	2	30,22	+ 0,02
	3		
	4		
	5		

32 ºC			
OT	№	AMP	Δ
31,8	1		
	2		
	3		
	4		
	5	30,75	- 0,05

34 ºC			
OT	№	AMP	Δ
34,4	1		
	2		
	3		
	4	34.46	+ 0,06
	5		

36 ºC			
OT	№	AMP	Δ
35,95	1	36.05	+ 0,1
	2		
	3		
	4		
	5		

37 ºC			
OT	№	AMP	Δ
37,15	1		
	2		
	3	37.10	- 0,05
	4		
	5		

Relative error of temperature measurement at different set temperatures is calculated by formula below:

$$\sigma_t = \frac{T_{MP} - T_{AMP}}{T_{MP}} \cdot 100 = \frac{\Delta}{T_{MP}} \cdot 100, \quad (1)$$

Where:

T_{MP} – temperature indicated by precision digital reference thermometer [ºC];

T_{AMP} – result of temperature measuring of AMP non-invasive screening analyzer [ºC];

$\Delta = T_{MP} - T_{AMP}$, [ºC] – data calculated by this formula shall be registered in Chart 6.

Criteria of conformity: $\Delta_{max} \leq 0{,}1$ ºC in range of temperature 24 °C – 37 °C.

15. Documentation of manufacturers' and periodic inspection

Should the inspection of analyzer has been successfully completed, manufacturer issues certificate of conformity and places label on sealing points of analyzer, indicating date and sign.

Should during inspection device do not meet conformity requirements, it is qualified as faulty and shall not be used.

16. Transportation and storage

16.1 Manufacturer or its authorized representative supplies the analyzer to the customer. Transportation of the properly packed analyzer is allowed by any transportation means in accordance with applicable rules for the transportation means.

16.2 Analyzer shall be kept in manufacturers' packing.

Warehouse shall be clean, free of dust, acid, alkali vapour or other dangerous components. Storage lifetime of device is one year maximum.

17. Warranty by manufacturer

Warranty period is 24 month for the device and 12 month for cable with 5 sensors counted from date of commissioning of analyzer, but not more than 30 days counted from the date of manufacturing.

Within a warranty period manufacturer will exchange the faulty device.

Should the seals are broken, or there are mechanical or chemical damages on the device, user lose the guarantee.

Over the guarantee period, all the works are to be paid to manufacturer in frame of separate contract.

18. Execution of destroying

After its rollout, analyzer shall be transported to manufacturer's site.

From the point of view of saving ecological environment, instead of destroying the device, it should be returned to the dealer.

19. Install the software

Be sure you have Administrator rights on your computer before installation.

19.1 Please, make sure that a computer has a free USB slot and any attached printer, before installation the program USPIH.

19.2 Put into a CD-ROM drive the purchased installation disk.

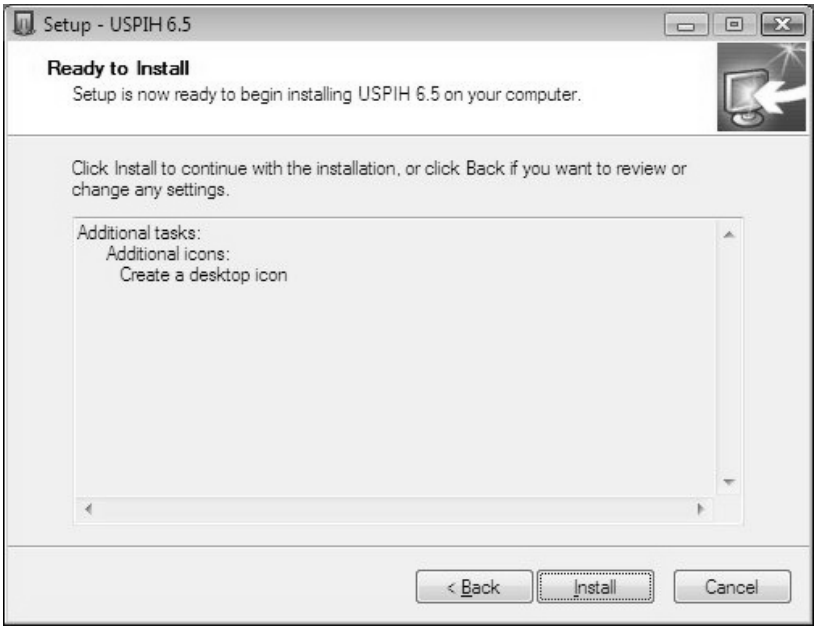
19.3 There will appear the following menu on your display. You can start installation when click by the inscription «*Run Setup_USPIH.exe*».

19.4 Select Setup language and press the button «OK»:

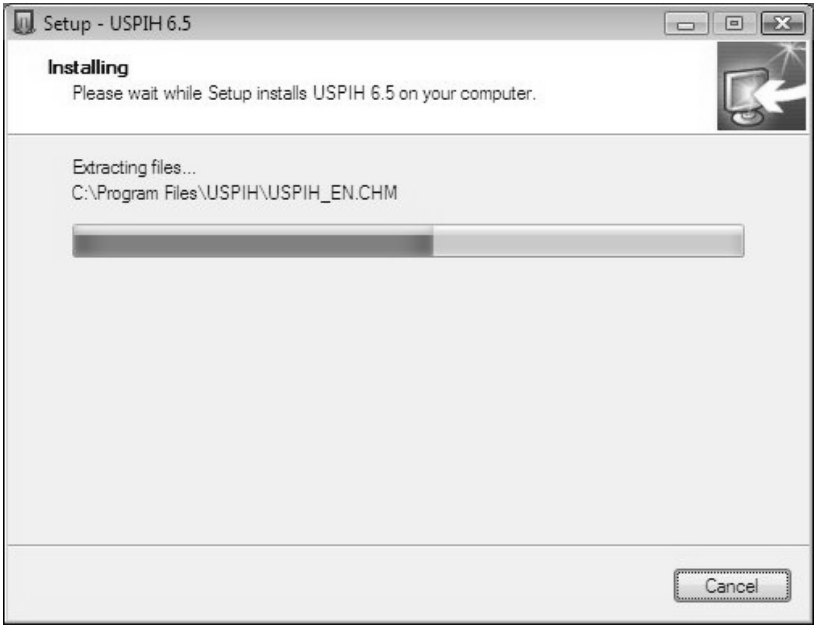
19.5 Press the button «Next >»:

19.6 Press the button «Next >»:

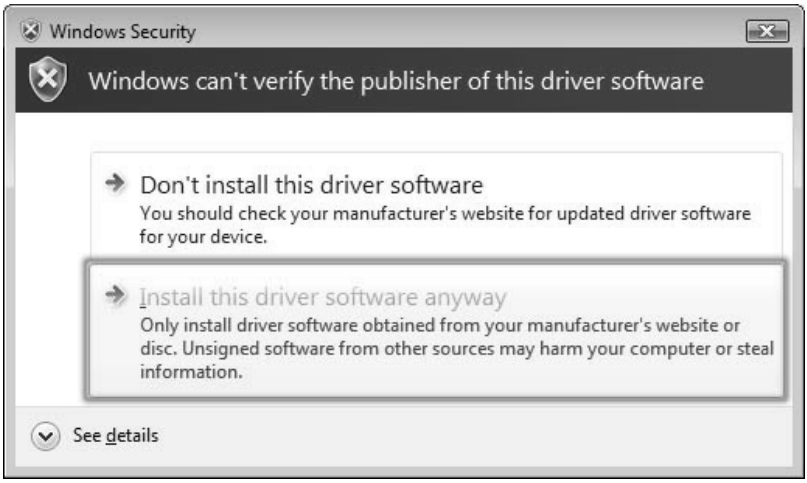
19.7 Press the button «Install»:



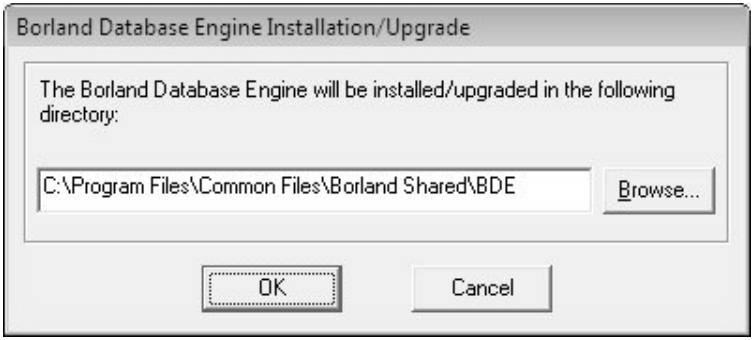
Please wait while Setup installs USPIH 6.2 on your computer.



19.8 Press the button «Install this driver software anyway»:



19.9 Press the button «OK»:



19.10 Press the button «Yes»:

19.11 Press the button «Finish»:

When the program is installed, there will appear the icons for starting the program USPIH 6.5 on the Desktop and in Quick Launch.

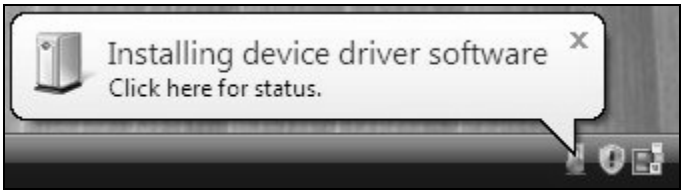
You are ready to connect up the device AMP and install the drivers.

20. Connect up the device AMP to a computer and install the drivers

20.1 You should prepare the device for connection to the computer:

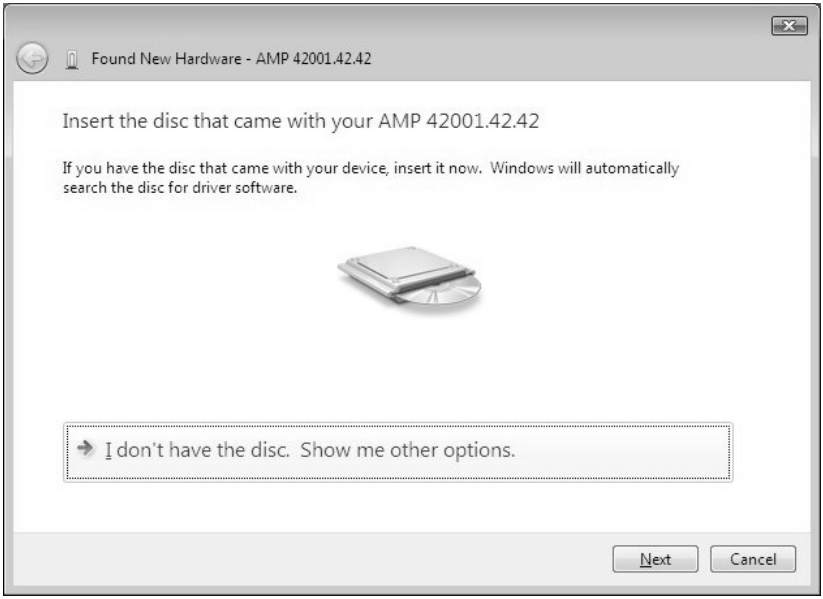
- link up the device AMP and cable with 5 micro-processors;
- connect the USB cable to the device;
- connect the USB cable to your computer.

You will see the following message on your display:



20.2 Press the button «Locate and install driver software (recommended)»:

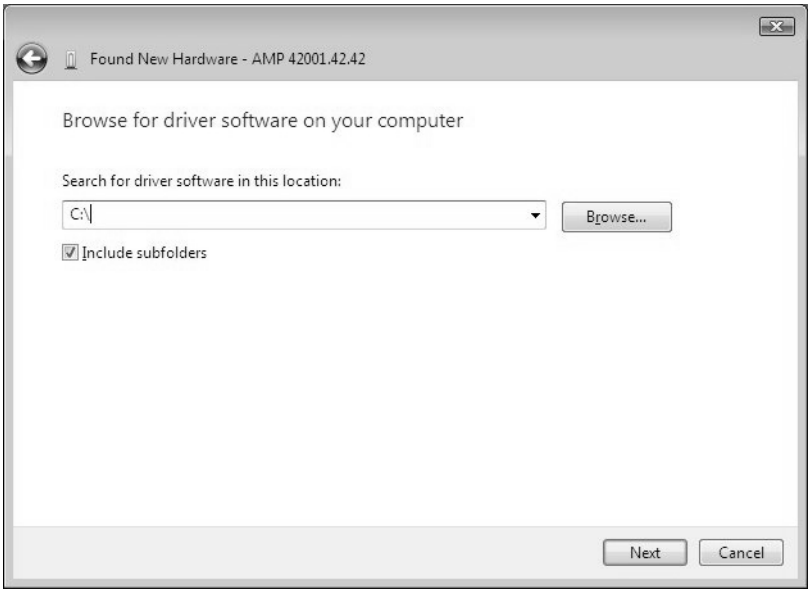
20.3 Press the button «I don't have the disc. Show me other options»:



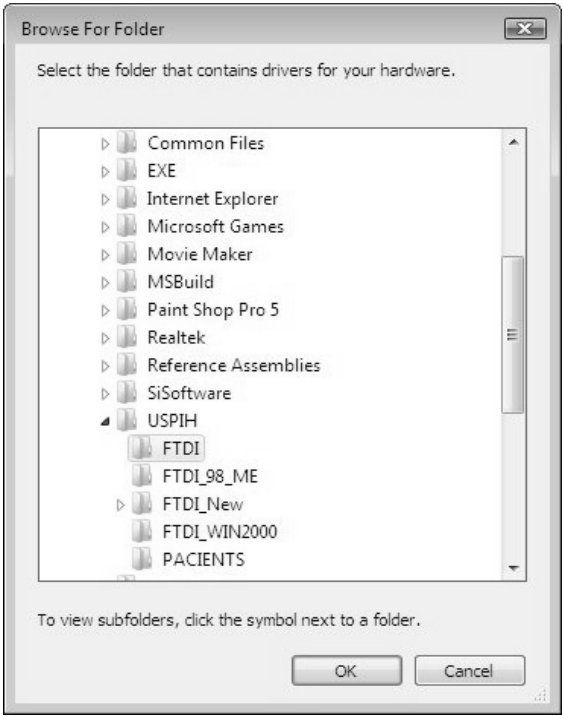
20.4 Press the button «Brows my computer for driver software (advanced)»:

20.5 In default, the drivers for connection the device AMP to your computer through USB interface are in the folder «C:\Program Files\USPIH» (select «Include subfolders»).

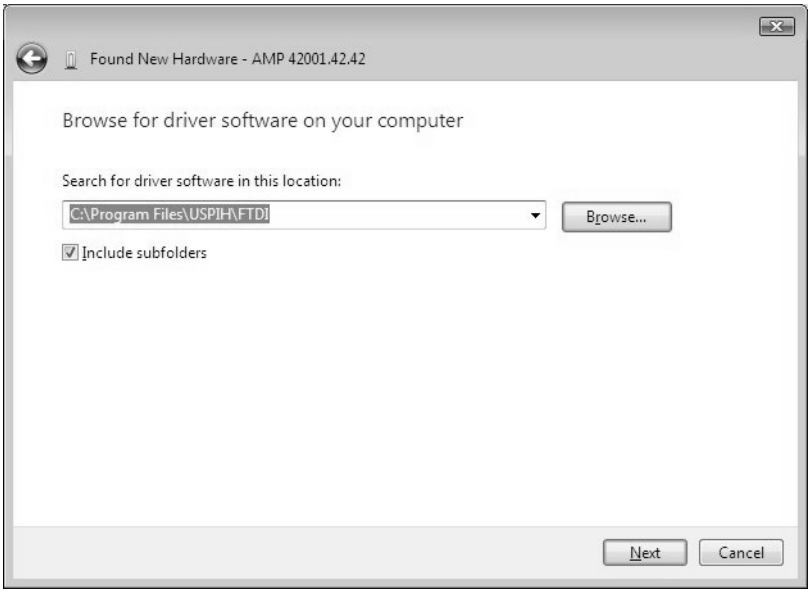
Press the button «Browse…»:



Select the folder «C:\Program Files\USPIH\FTDI»:

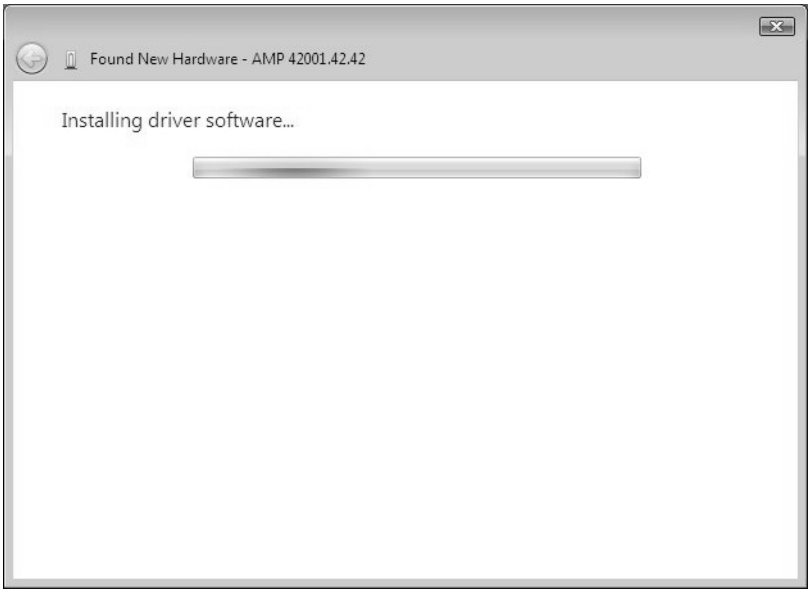


Press the button «Next»:

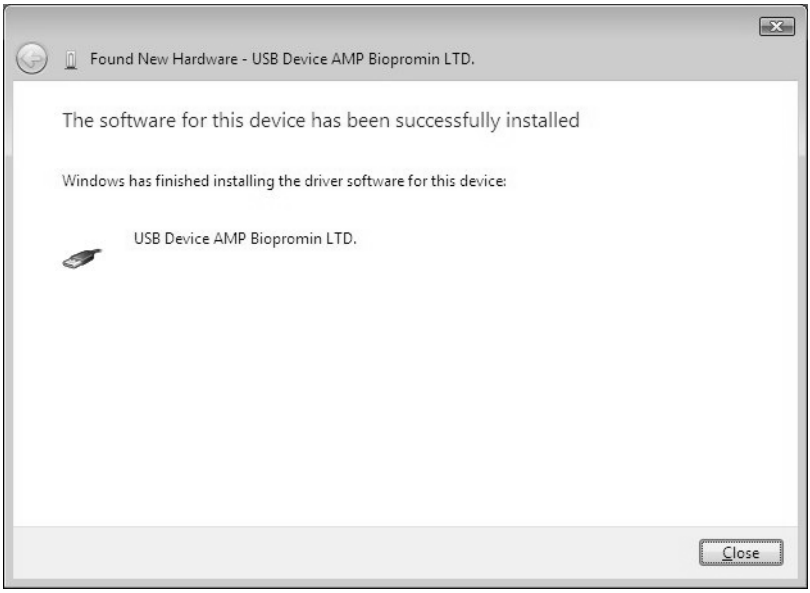


20.6 Press the button «Install this driver software anyway»:

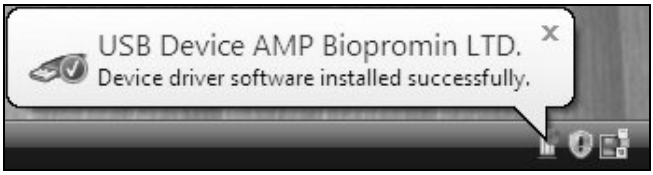
Installing driver software...



20.7 Press the button «Close»:



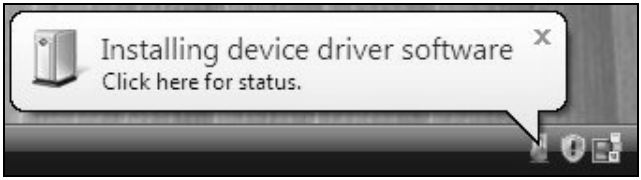
The following message will appear at the desktop:



If you device was completed with special key Guardant Stealth II.

Put Guardant Stealth II into a USB slot of your computer.

The following message will appear on your display:

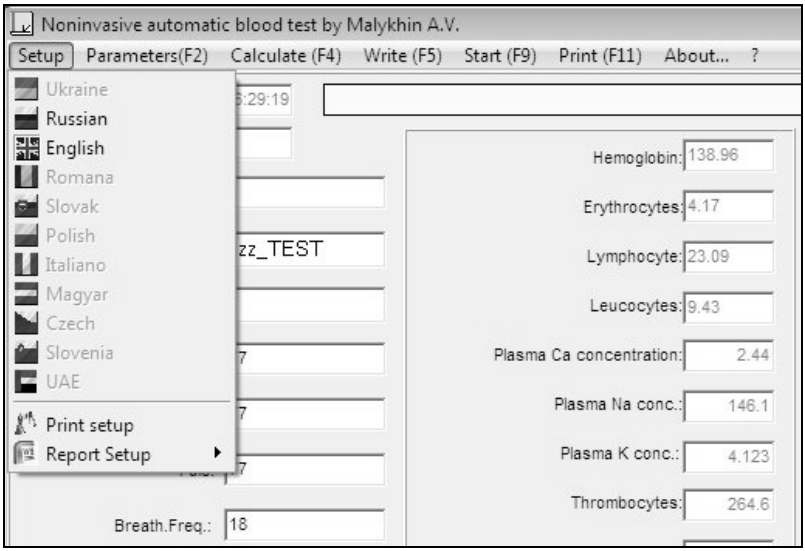


The process of connection up the device AMP to your computer and installation of all drivers is finished. So you can pass on to adjustment of the program USPIH.

21. Setup the program USPIH

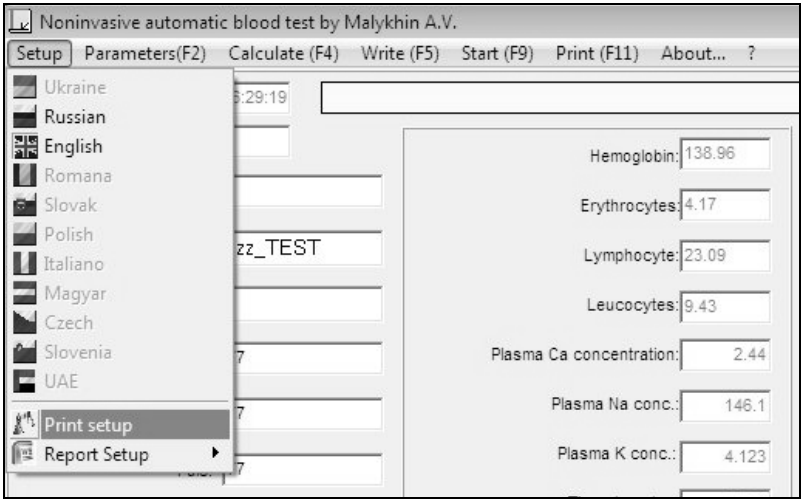
21.1 Please, start the program.

21.2 The program will start in English:



21.3 Setup a report of diagnostics for printing:

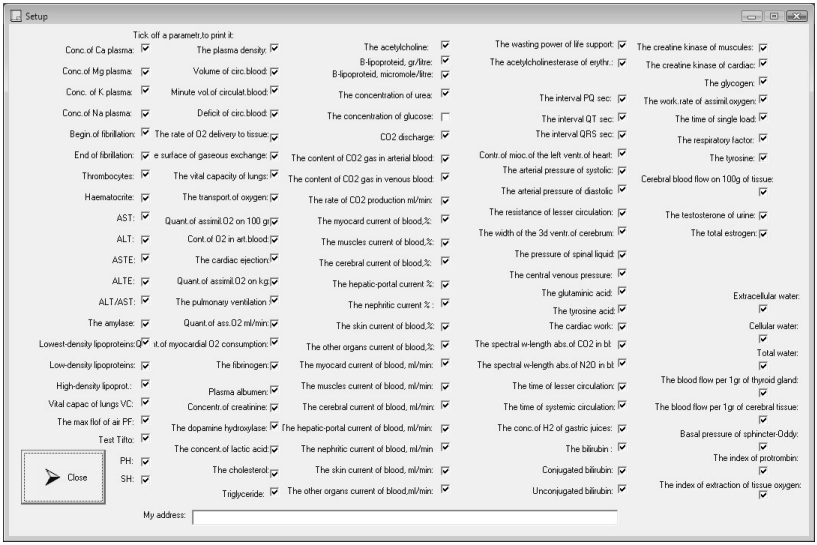
To make more detailed setup of a report, open in a menu "Setup"->"Print setup".



There will be displayed a panel «Print setup».

Tick off the results you want to print. Your Essential Elements (the name of a company, telephones, etc) will be printed in a heading of report. You can adjust the Essential Elements across using space bar.

Then, press the button "Exit" and a panel "Print setup" will be closed. All changes will be saved and take effect only after leaving a panel "Print setup".



Then you are ready for a work with the program US-PIH.

22. Work with the software

22.1 A description of the program USPIH interface.

22.1.1 The menu

"Setup"- use to setup an interface language and detailed setup of a diagnostic report.

"Parameters(F2)" - use to display a panel with additional parameters.

"Calculate(F4)" - use to define a blood formula and additional parameters by hand.

"Write(F5)" - use for checking a completeness of the database before the program USPIH ends of working.

"Start(F9)" - use to start up the device AMP and to begin measuring.

"Print(F11)" - use for preparing and printing a report with defined parameters of blood formula, etc..

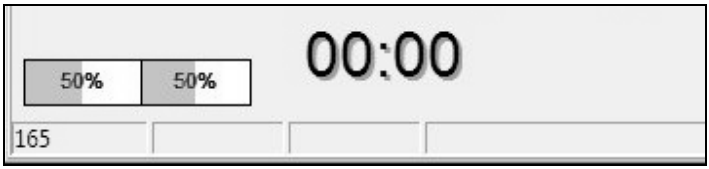
"About..." - it is short information about the program...

"?" - use to open a Help file.

F1 – use to open a Help file.

F6 – use to select Standard panel or CE panel.

22.1.2 Timer



It is used for calculation of patient's heartbeats by hand.

The Timer starts working when you click the left button of a mouse on "00:00". After that, it works 3minutes and stops automaticaly.

22.1.3 Other controls

When you press this button, all records in the database of patients will be rewrited. In other words it'll be carried out indexation of the database. Also, all patient's cards will be checked whether they were filled in right (Are they complete or not?).We recommend you to make a Record at the end of the work with the program. If there are any errors in database, the program will stop on a wrong patient's card and suggest deleting it. We recommend you to follow the program’s instructions.

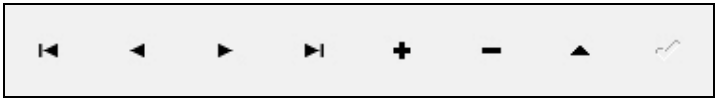
When you press this button, the program makes a calculation of parameters (it defines them). The definitions will be made automatically,

but if it is necessary to specify (correct) weight, pulse or smth else, you should press the button above.

To save an information about patient in the database  .

When you press this button, you will leave the program.

These are buttons for navigation through records in the database:



 pass on the first records in the database.

 pass on the last records in the database.

 pass to the previous records in the database.

 pass to the next records in the database.

 pass to the next or previous records in the database.

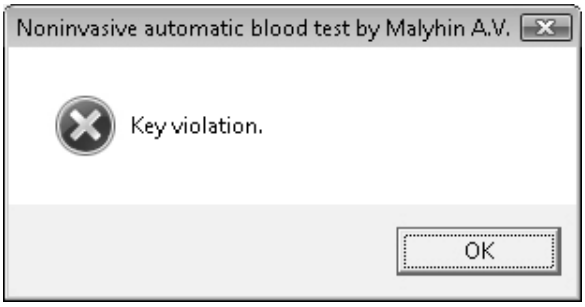
 delete a patient's card.

 edit record.

 save information about patient in the database.

ATTENTION! To save information about patient in the database, you should OBLIGATORY press this button after testing a patient and manual definition of blood formula

ATTENTION! Unfortunately, the database supports only unique name of records. So, if you have already had a patient Ivanov Ivan in your database, you will not save another patient with the same name. There will be displayed the following window:



In that case, you can write in the field "Name" - Ivanov Ivan 2 or Ivanov Sergey, etc. So, you can see that the patient Ivanov Ivan come to test repeatedly and Ivanov Sergey was another patient.

Attention: when you add a new patient and press the button  , the program adds the unique number after every name. Please, DON'T DELETE IT and all records will be unique in your database.

22.2 How to fill in a patient's card

Please, fill in the following fields:

Remark - This field is for short overhead information (optional information). For example, from which clinic or hospital a patient is.

Name - Patient's name and surname.

Sex - male (man) or female (woman) Attention! You should write only a letter m or M, w or W. It is recommended write a figure 1 – for male, and figure 0 – for female. Please, don't try to put any other letter!

Age - complete number of years (from 6 till 99).

Weight – complete number of weight (kilogram).

Puls - quantity of heartbeats during 60 seconds. (You must define it exactly!) You can use pulse sensor "POLAR", if you have any problems with definition of heartbeats' quantity by hand. You can order this sensor in our company or buy it yourself.

Breath. *Freq*. - quantity of breathes during a minute.

Diagnose – A diagnosis (or complaints) that a patient has before examination. This field supports 250 symbols. So, write shortly, please.

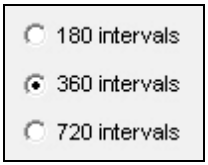
IT IS IMPORTANT! Don't fill in other fields. They will be completed automatically.

22.3 Put the microprocessors on a patient, each color for corresponding field:

BLUE	- on the bifurcation of aorta, at the left side, in the area of cricoid's cartilage.
GREEN	- on the bifurcation of aorta, at the right side, in the area of cricoid's cartilage.
YELLOW	- in the left axillary crease (like a thermometer).
VIOLET	- in the right axillary crease (like a thermometer).
RED	- on the umbilicus (navel). If a patient hasn't a navel, you should put the microprocessor to the region, where the navel was before surgery.

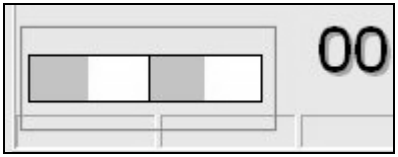
22.4 Press the button F9 on your keyboard or "START" in the menu. An information processing will be begun. It will last 360 sec, and blue line will show a progress of the device working.

An interval of examination (in default, it is 360sec).



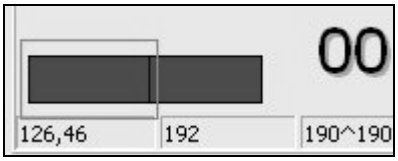
An interval of examination can be changed during the process of the device working. You should pay attention to the color of temperature figures, **they couldn't be red**! If some of them s red, this microprocessor was put in wrong way. Put it again.

From version USPIH 6.4 interface of the program was changed. There were added the indicators of 5-microprocessors' application accuracy.

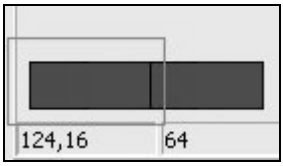


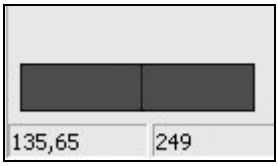
The first indicator changes its color from red to green when:

-the difference between temperatures in fields of left and right carotid artery bifurcation is less than 0.5°C;
-the temperature in 5 fields becomes stable;

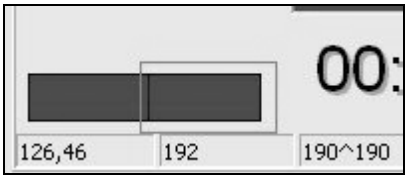


Otherwise the indicator is red.

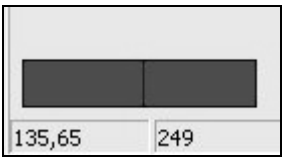


or


The second indicator changes its color from red to green when: the difference between temperatures in fields of left and right axillary creases is less than 0.5°C, the temperature in 5 fields becomes stable.



Otherwise the indicator is red.

or


When the process of examination is finishing, you can see the following notice on the bottom of the panel.

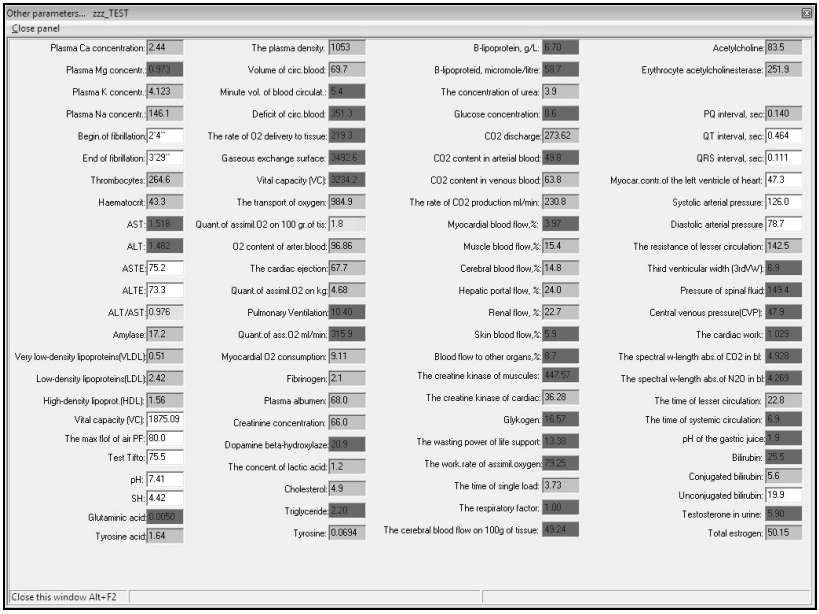
Different numbers could be there, but they must be nonzero.

If any number is zero, you should choose larger interval for the examination (for example, you examination was 360 sec, you should choose 720 sec interval in such case).

When the progress of examination is 100%, all fields of patient's card will be completed. The progress line will disappear. Hemogram fields will be completed too.

IT IS IMPORTANT! Please, remember a blood formula, in itself, gives not enough information about the state of patient and prognosis for a disease.

22.5 To display the additional parameters of diagnostic press on your button F2 or "Parameters(F2)" in menu. A panel with additional parameters will appear.



This panel has colored windows:

- red – the parameter is higher or lower than norm;
- blue – the parameter is normal;
- white – the parameter doesn't compare with norm;
- yellow – the parameter doesn't satisfy the norm.

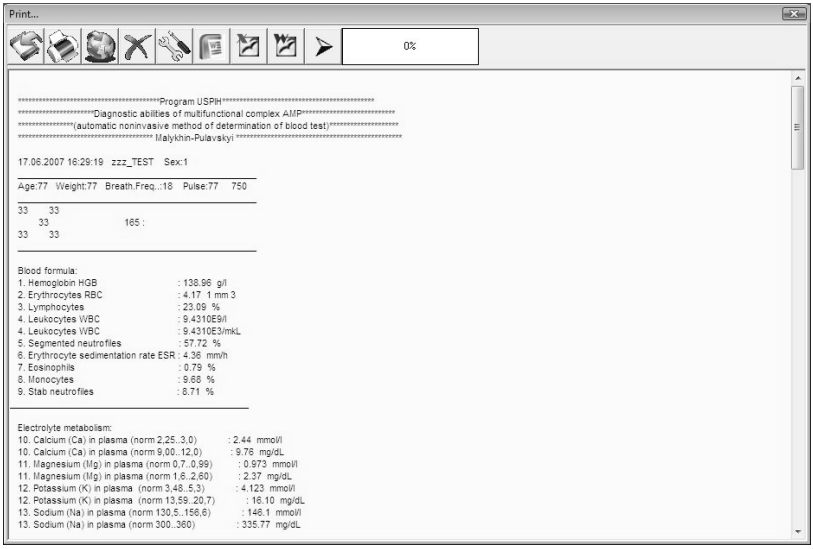
IT IS IMPORTANT! Please, remember there is no one person with used norms of all parameters in nature. These parameters were received many years ago, in limited study population. They are average statistical.

IT IS IMPORTANT! Additional parameters help to estimate a patient' state more exactly and make a prognosis for a disease, prescribe medicine.

You can close this panel use keys ALT+F2, when you have studied all additional parameters.

22.6 To prepare a report for printing, please, press key F11.

When you press the key F11, there will be displayed a window of report editor. There is a computer prompting of presumptive diagnosis for a doctor at the end of a report. A doctor can agree or not with it, add or delete something from it or delete at all (print a report without it for patient).



IT IS IMPORTANT! Please, remember: only a doctor can diagnose a patient! A computer gives a prompting from a list of diagnosis from its memory. So a computer doesn't know all nosology now!

22.7 Saving results of diagnostics in file or print copy.

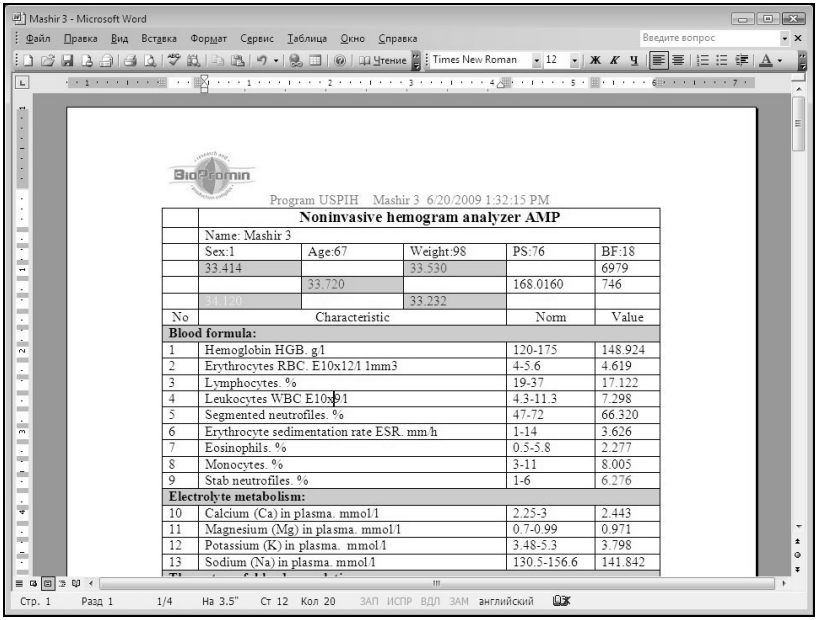
To save results of diagnostics in file, please, press the button  and save it.

To print results, please press the button  .

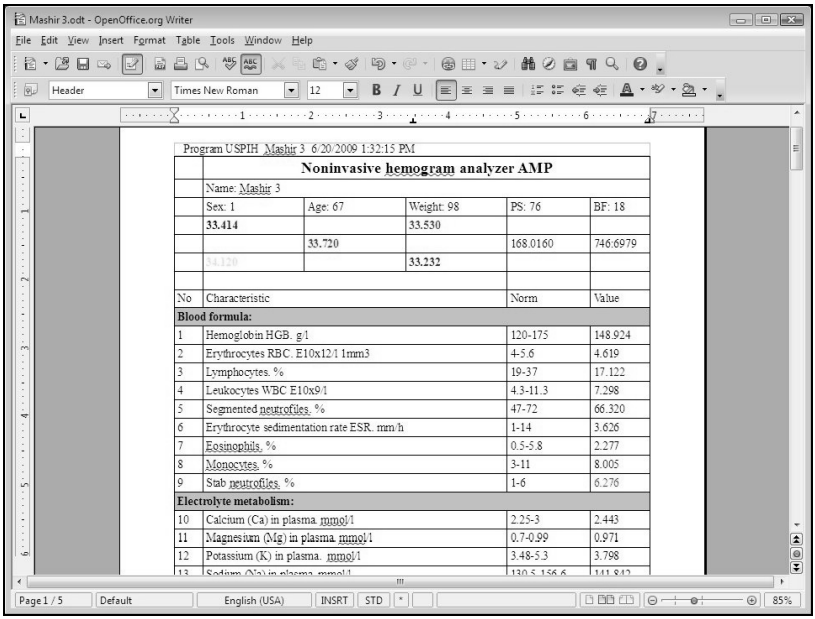
Cleaning a report editor :  .

Selection of a font:  .

Press the button  to export results to MS Word. The program exports results of diagnostics to MS Word and will start it:



Press the button  to export results to the Open Office Writer. The program exports results of diagnostics to the Open Office Writer and will start it:



Program USPIH Mashir 3 6/20/2009 1:32:15 PM

Noninvasive hemogram analyzer AMP

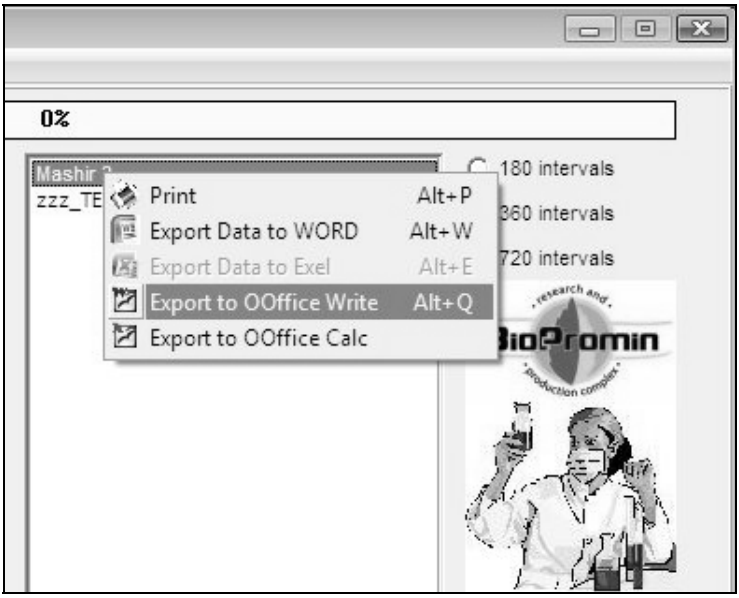
Name: Mashir 3

	Sex: 1	Age: 67	Weight: 98	PS: 76	BF: 18
	33.414		33.530		
		33.720		168.0160	746:6979
	34.120		**33.232**		
No	Characteristic			Norm	Value
Blood formula:					
1	Hemoglobin HGB. g/1			120-175	148.924
2	Erythrocytes RBC. E10x12/1 1mm3			4-5.6	4.619
3	Lymphocytes. %			19-37	17.122
4	Leukocytes WBC E10x9/1			4.3-11.3	7.298
5	Segmented neutrofiles. %			47-72	66.320
6	Erythrocyte sedimentation rate ESR. mm/h			1-14	3.626
7	Eosinophils. %			0.5-5.8	2.277
8	Monocytes. %			3-11	8.005
9	Stab neutrofiles. %			1-6	6.276
Electrolyte metabolism:					
10	Calcium (Ca) in plasma. mmol/1			2.25-3	2.443
11	Magnesium (Mg) in plasma. mmol/1			0.7-0.99	0.971
12	Potassium (K) in plasma. mmol/1			3.48-5.3	3.798
13	Sodium (Na) in plasma. mmol/1			130.5-156.6	141.842

Press the button:  to export result to the Open Office Calc

Leaving a panel "A report of diagnostics:  .

The same functions can be caused by means of the contextual menu. Click the right button of a mouse on corresponding record and choose necessary application:



22.8 End of working with program USPIH

When you finish working with program USPIH, choose in a menu "Write F5" or press the following button: 

.

If any patient's card has been filled wrong, there will be displayed the following window:

Press "OK". There will be displayed a confirmation for deleting a wrong card:

Please, confirm deleting a wrong patient's card and press "OK". A card will be deleted.

If there were some wrong cards in your database, you should do actions described above till all wrong cards are deleted.

To close program USPIH, press the button: 

.

22.9 Calculation of examinations' quantity (not for all versions of the device).

The program calculates examinations' quantity automatically. You can see a quantity of remaining examinations (till software update) at the right corner of status bar:

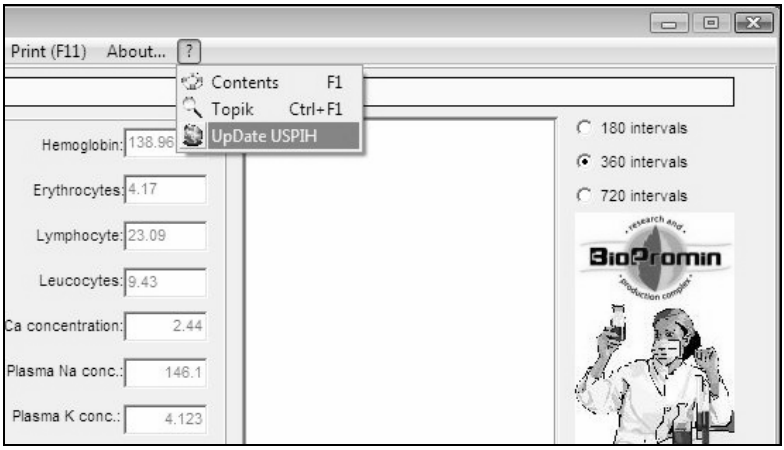
There are 9 more examinations in this example. As a quantity of remaining examinations is less than 10, a status bar is red.

ATTENTION! If status bar of the program USPIH has changed its color to red, please, connect with your provider of the program and device AMP for renewal your GUARDANT key (look part 25). Let him know the number of your device and exchange your GUARDANT key for new one (with updated software).

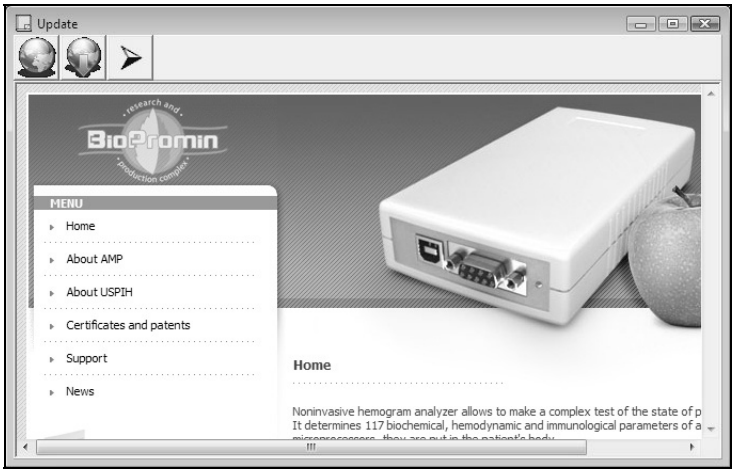
NOTES: If the remaining quantity of examinations is "0", the program USPIH will not work (you couldn't examine new patients).

23. How to update the software

23.1 To update the program «USPIH» click «?» and choose «UpDate USPIH».

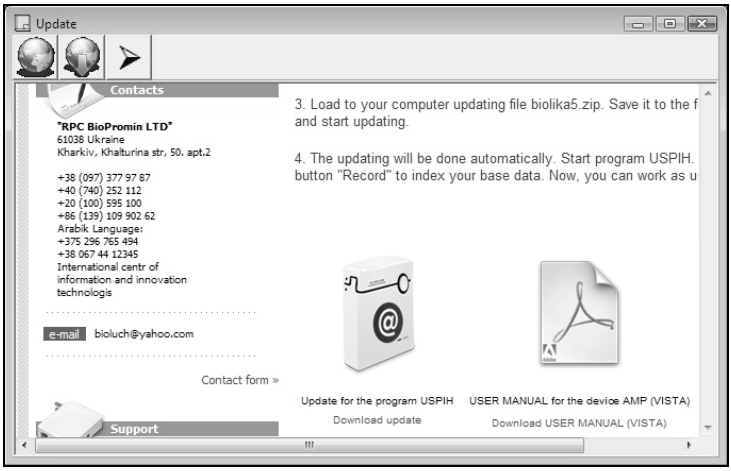


Click on the button  in the appeared window. You will be re-directed to a web *http://www.analizator-amp.com.ua/en/.*



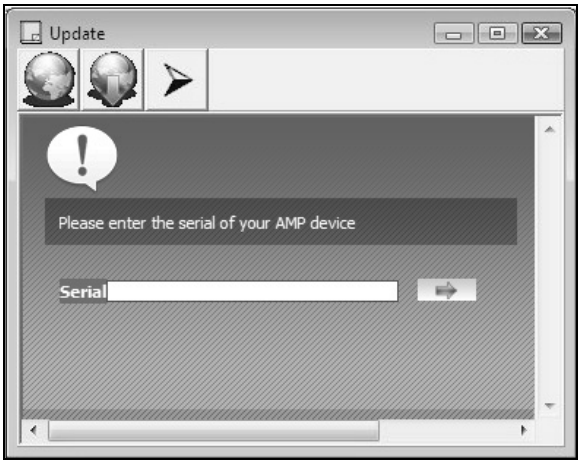
Choose the tab «Support». Then click «How to update the software».

Click on icon «Update for the program USPIH».

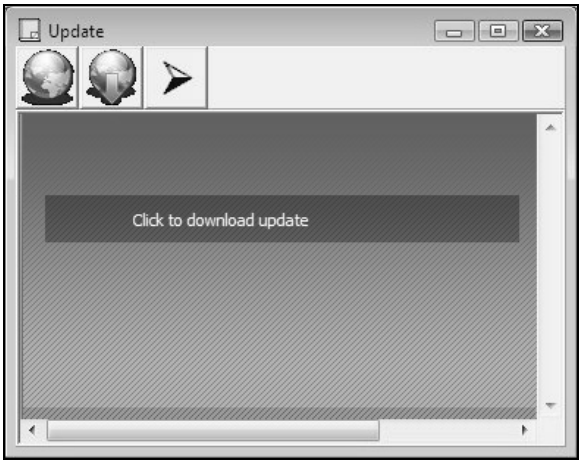


Press the button  if you want to open a loading window immediately.

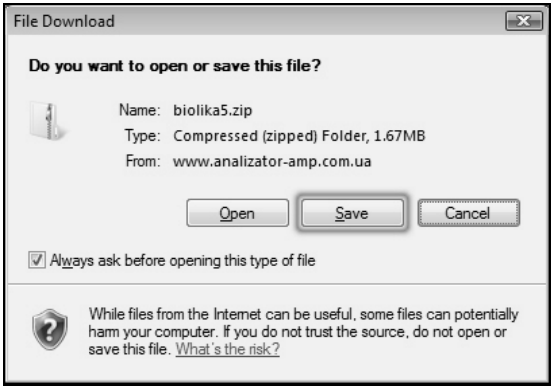
Put the serial number (for example 38081010) of you device AMP and press an arrow:



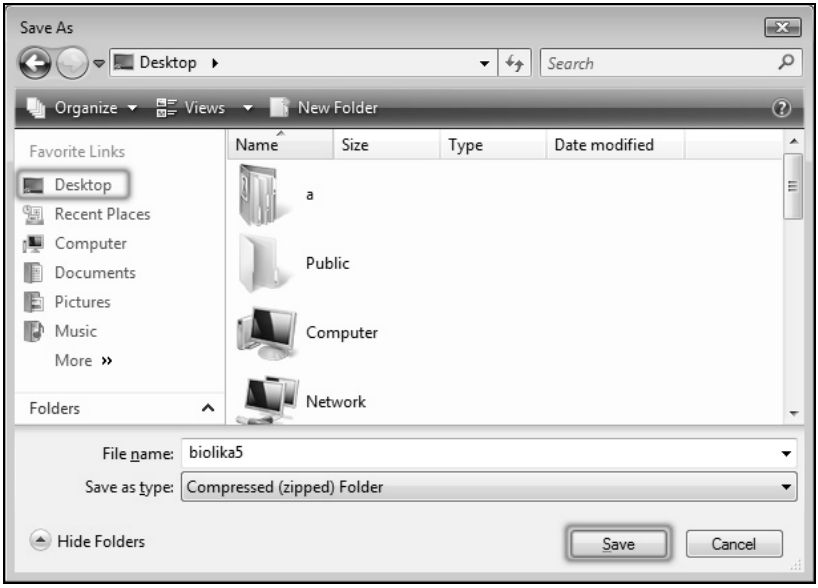
Press the link:



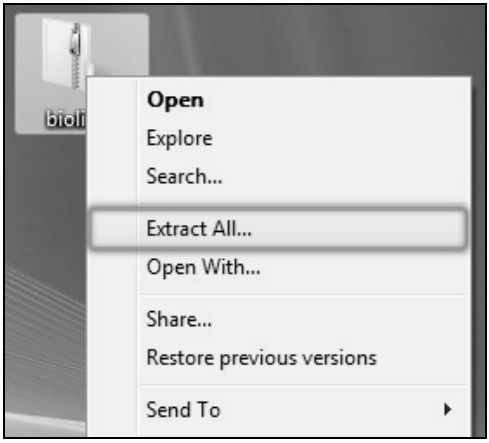
Press «Save»:



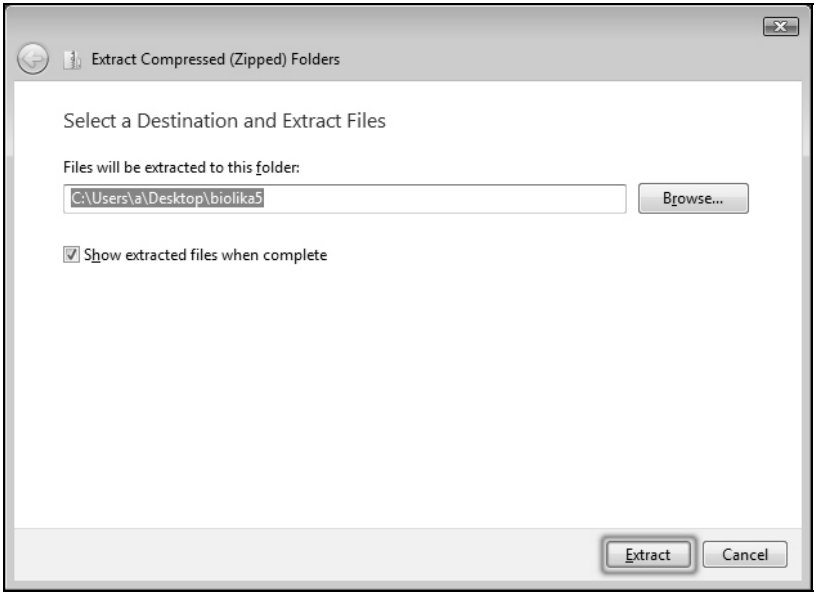
Select a folder for saving (for example, Desktop). Press «Save»:



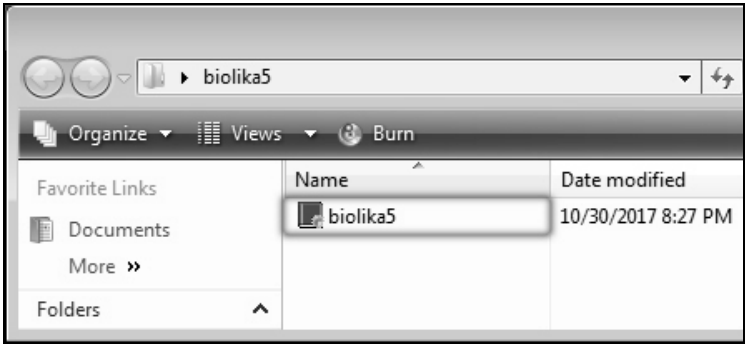
When the file “biolika5.zip” is downloaded, unpack it please.



Please, press «Extract»:

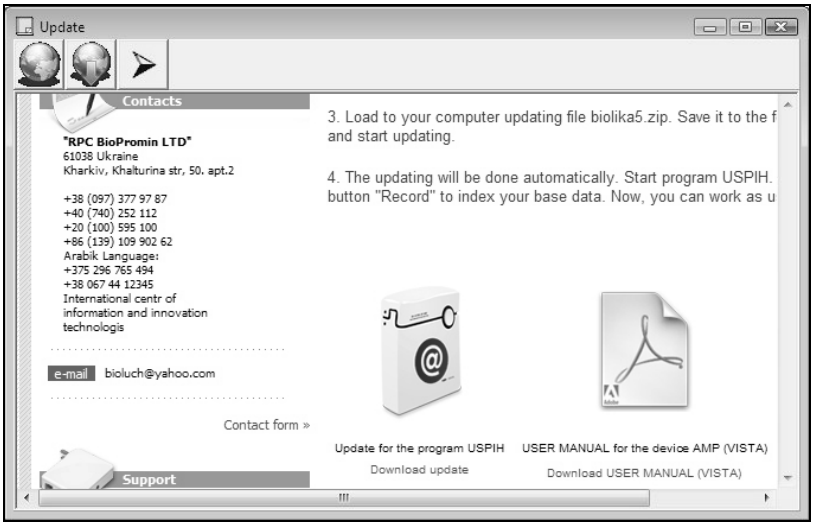


A folder with program update will open:



Start updating. There is the detailed description of this process in the part «Install the software».

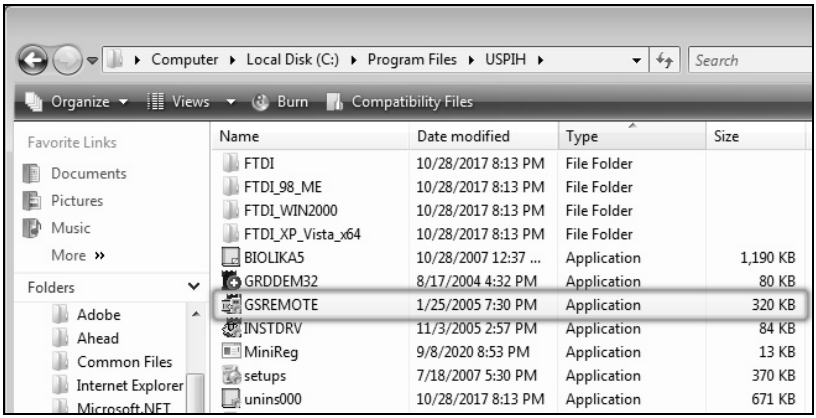
23.2 To receive the user manual for the device AMP, click on the same icon and save the manual like it is described in part 24.1.



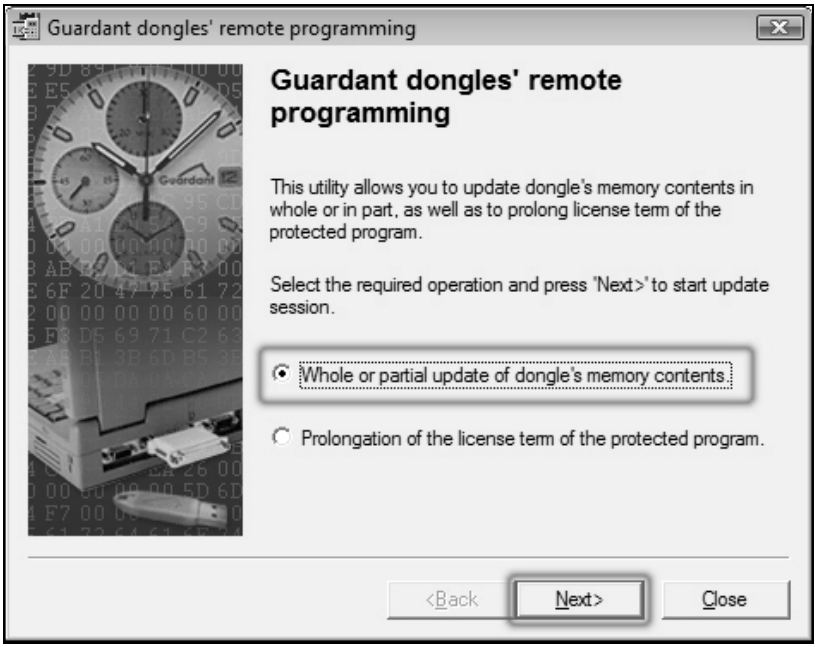
24. Update GUARDANT key

You can update your GUARDANT key yourself. You should do the following:

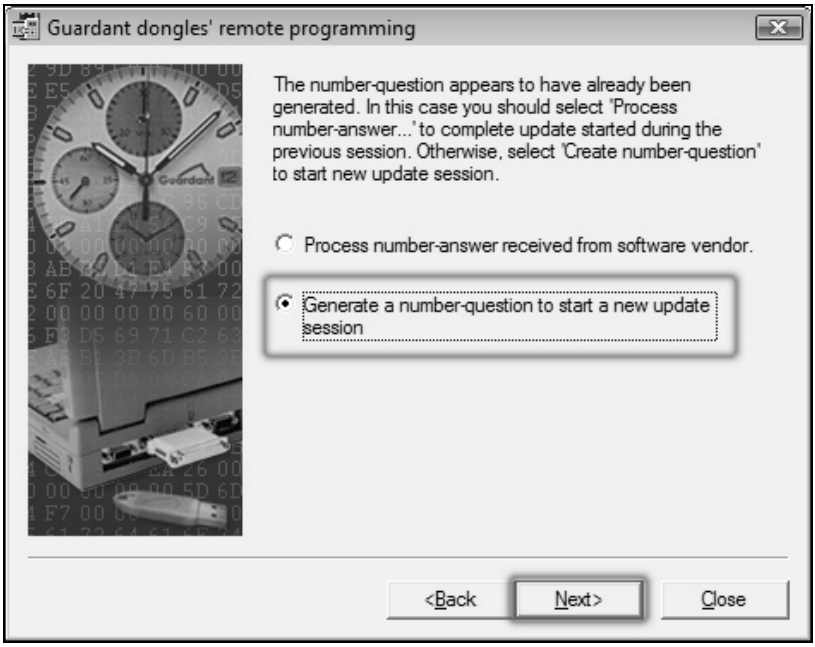
Open «C:\Program Files\USPIH», start the GSREMOTE.EXE application.



Press the button «Next»:

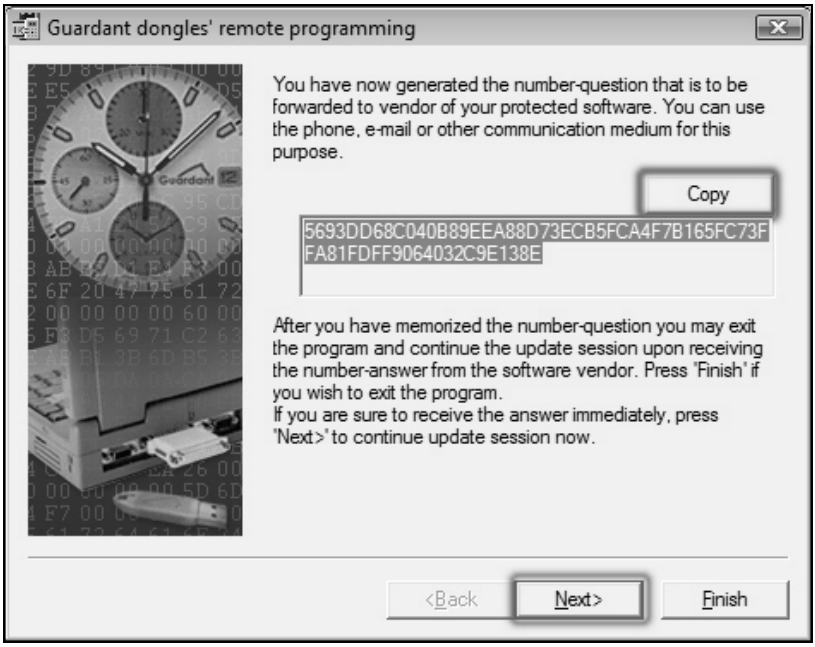


Press the button «Next»:

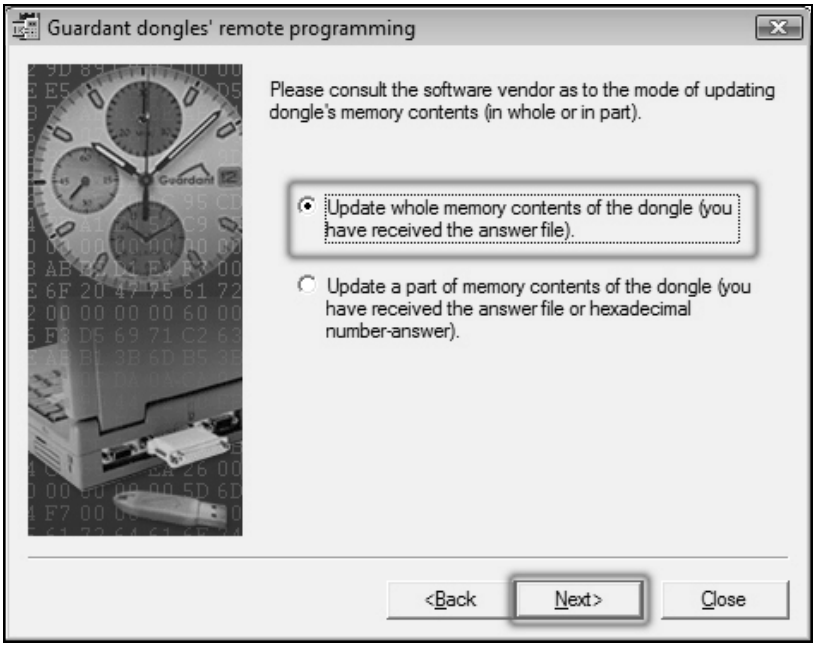


Press the button «Copy» and send a number-question to e-mail which you can find on ***http://www.analizator-amp.com.ua/en/*** or send it to ICQ: 259-030-294 (in following example the number-question is «5693DD68C040B89EEA88D73ECB5FCA 4F7B165FC73FFA81FDFF9064032C9E138E»)

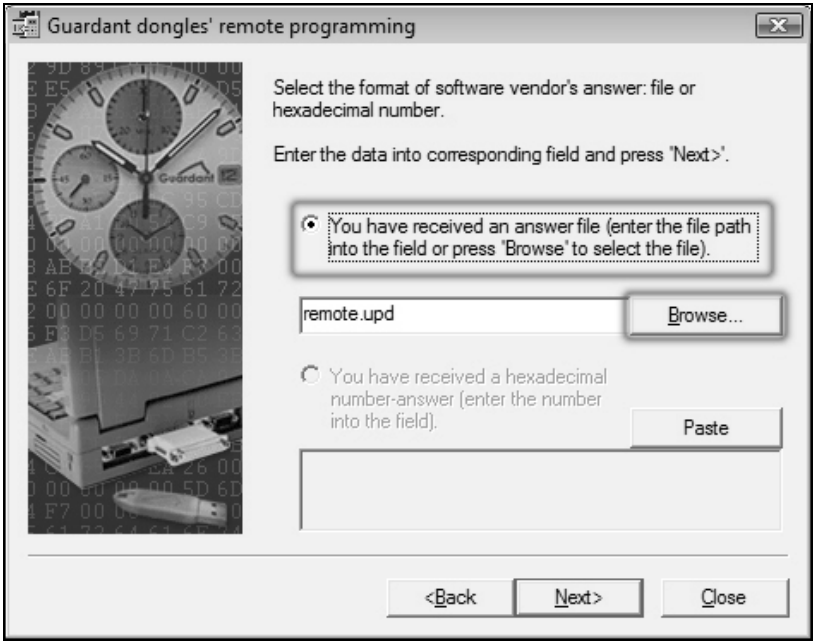
Press the button «Next»:



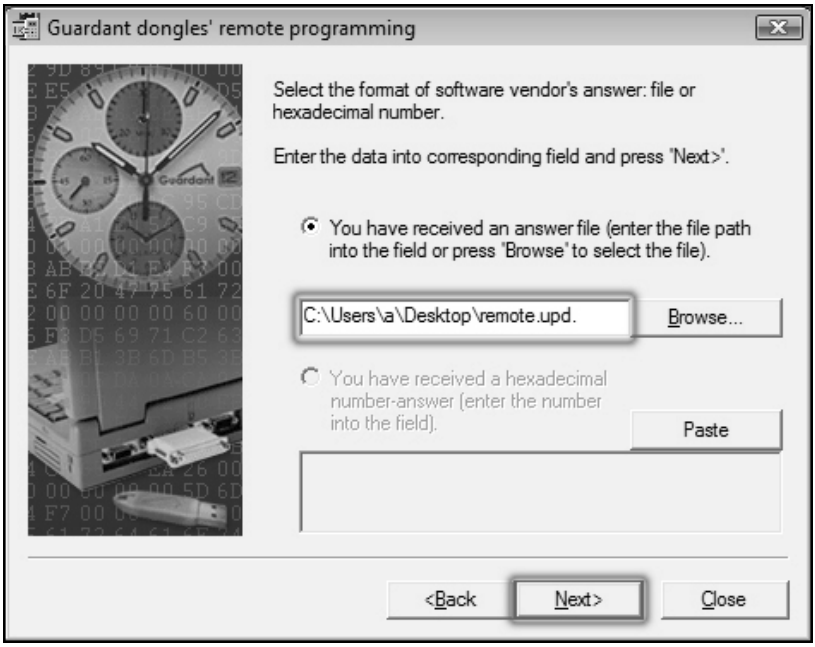
Press the button «Next»:



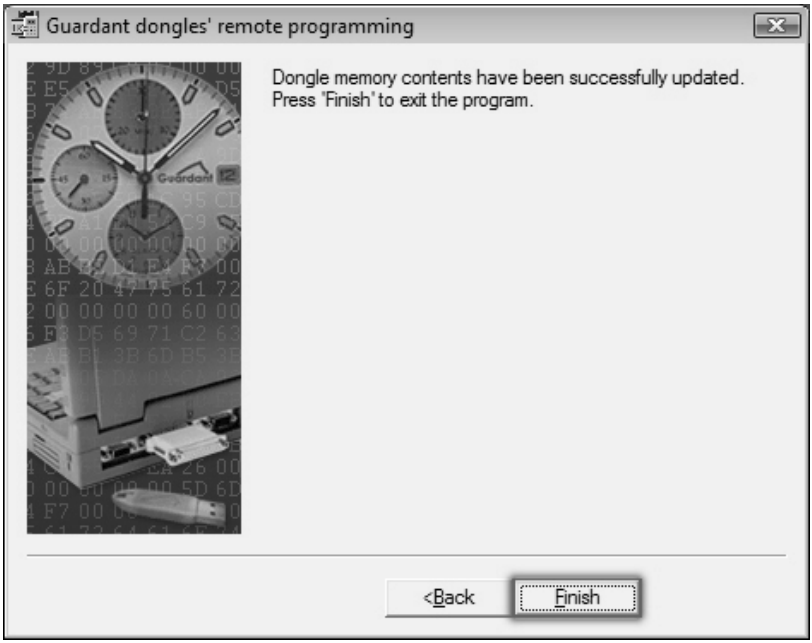
You will receive by e-mail an updated file “remote.upd”. You should press the button «Browse...» and specify a path to file “remote.upd”.



Press the button «Next»:



If you see the following window, your GUARDANT key is successfully updated. Press the button «Finish»:



Dongle memory contents have been successfully updated!

You can buy a version of the device without examination accounting.

25. Possible problems and troubles

25.1 Problem: After installation the program USPIH, program doesn't work.

Solution:

a) Please, check whether key Guardant Stealth II connect with computer (through USB-port):

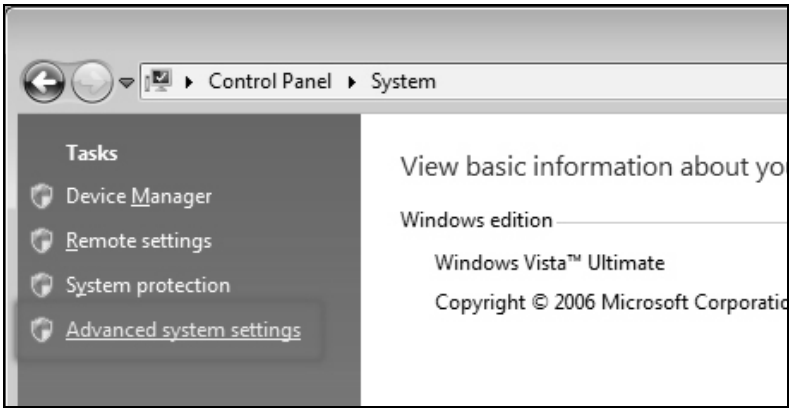
b) There should be light inside your key (there is a LED inside). If there is no light, you didn't install the driver for Guardant Stealth II. Please, install it.

c) You should check whether the driver for Guardant Stealth II was installed right.

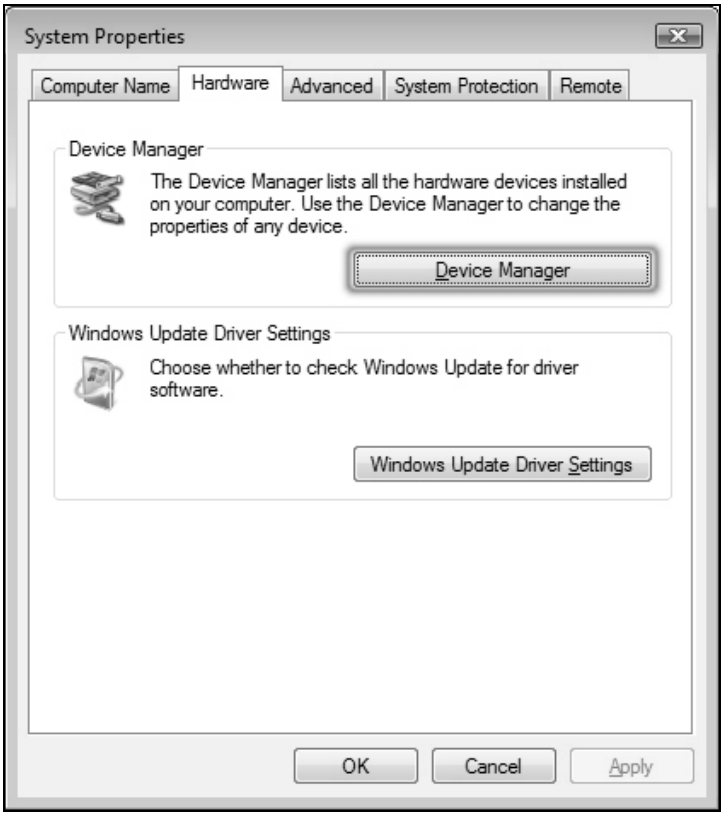
Open the «Control Panel»:

Run the «System»:

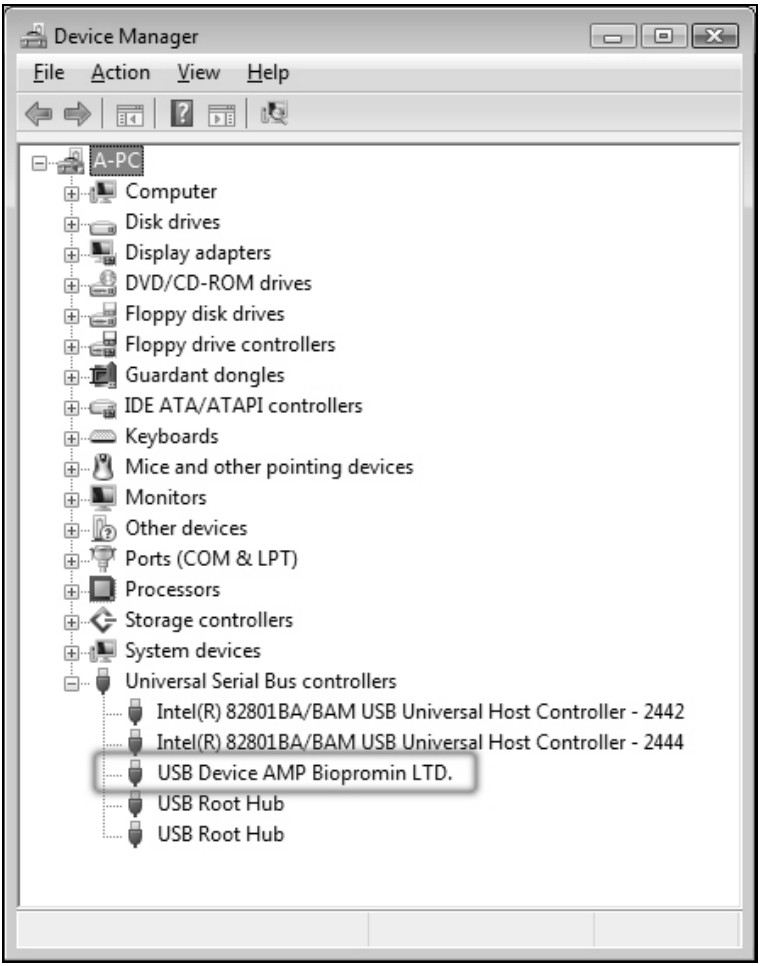
Select «Advanced system settings»:



Select «Hardware» and «Device Manager»:



Check whether controllers were installed right:



If they were installed wrong or ill-worked, please install them once more.

25.2 Problem: LED on the front panel of the device is blinking

Reason: the cable with 5 microprocessors is damaged.

Solution: Let your provider know that and ask him to exchange damaged cable with 5 microprocessors for new one.

NOTES: The exchange of cable with 5 microprocessors will be realized only in a complete with your device AMP and Guardant Stealth II key.

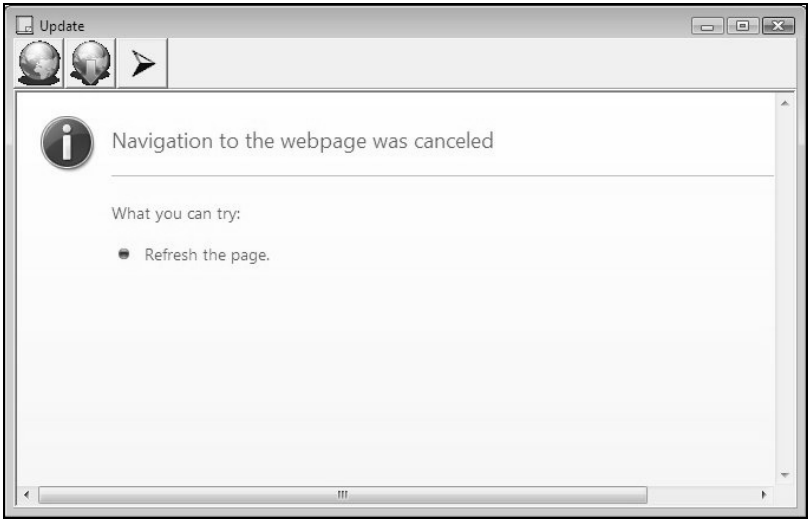
25.3 Problem: After starting the program USPIH the following panel appears:

Solution:

a).The device AMP hasn't connected to your computer. Connect it, please.

b). A USB-cable is damaged, please exchange it.

25.4 Problem: At attempt of updating the window looks like:



Solution: Check up connection options to the Internet.

26. Description of metabolic and biochemical indices, covered by Malykhin-Pulavskiy USPIH Software

Electrolyte metabolism:

10. **Calcium** is a cation, constituting a part of blood cells and electrolytes. Its normal concentration in the blood plasma ranges from 2.02 to 2.2 mmol/l. It is regulated by parathyroid gland, bone tissue and pituitary thyrotropic hormone. The regulation of calcium in the organism is attained by triiodothyronine and tetraiodothyronine metabolism optimization, as well as by creatinine kinase of the muscles and heart.

11. **Magnesium** is a cation, constituting a part of blood cells. Its primary functional purpose is participation in the development of conductivity and contractility of those muscles, constituting a part of vascular wall. Magnesium normal value ranges from 0.7 to 1.0 mmol/l. It is regulated by the activation of creatinine phosphatase phosphorylation. In case magnesium level is less than 0.7 mmol/l, clinical picture of the disease is characterized by neuromuscular hyperexcitability, spasmophilia, and asthenic feelings.

12. **Potassium** is a cation, being presented in the blood plasma in the concentration 4.14 – 4.56 mmol/l. Its primary functional purpose is to participate in the neuromuscular conductivity. The gastrointestinal tract and kidney play a significant role in the regulation of potassium metabolism. Hypokalemia threatens with severe consequences. It may be observed in Conn's syndrome and can accompany occasional myoparaly-

sis, combined with migraines, epilepsy, and progressive muscular dystrophy. Hypokalemia can appear as a result of potassium loss through the gastrointestinal tract and kidneys, and due to the diabetic acidosis. Hyperkalemia is associated with the cardiac and renal malfunctions.

13. **Sodium** is a primary cation in the blood plasma. Its normal value is 130.5 – 156.6 mmol/l. Changes in the concentration relate to the changes in plasma specific conductivity, which normally makes up 0.72 +- 1 Ohm/cm. Changes to the regulation of sodium in the organism are associated with kidney diseases, gastrointestinal disturbances, as well as with the impairment of contractility. Rise in venous blood pressure causes hydrostatic pressure to increase. When hydrostatic pressure is higher than oncotic pressure, this can cause electrolytes out of intercellular space. This phenomenon leads to hypovolemia and activates juxtaglomerular apparatus of kidneys. This results in stimulation of the adrenal cortex and increase in aldosterone secretion. In a whole, these factor combinations give rise to the organotrophic disorder. All these factors bring on changes in the diurnal diuresis.

The system of blood fibrillation:

14,15,16,17 The most important factors of this system are plasma kinins. Practically, they form kinin system, which supports regulation of the local and general blood circulation, as well as vascular permeability. The main mechanisms are interactions between plasma kallikreins and tissue kallekreins (of pancreas, salivary glands, kidneys and intestinal wall). As the final result,

this interaction leads to the beginning and to the end of blood fibrillation. It is observed that there should be an interval, exceeding 30 seconds, between the beginning and the end of blood fibrillation. The platelets (containing arachidonic acid) play an important role in the formation of this time interval. Haematocrite is of considerable importance in the formation of interval between the beginning and the end of blood fibrillation.

The fermentative system:

18,19,20,21,22 AST and ALT are enzymes catalyzing intermolecular amino group transfer between amino acids and keto acids. As a result of the interaction between these transferases, oxaloacetic, pyruvic and glutamic acids. Elevations of aminotransferase activity, especially of AST, are observed in the myocardial diseases. Elevations in ALT activity is observed in viral hepatitis type A. Besides, elevation of ALT activity is seen with acute myocardial infarction, but this elevation is not so sharp, as compared to AST activity. Simultaneous determination of these two aminotransferases is a very valuable diagnostic test. In health, AST-ALT activity ratio (de Ritis coefficient) equals to 1.33+- 0,42. This coefficient reduces in the patients with viral hepatitis and rises in the patients with acute myocardial infarction.

23. **Amylase** is an enzyme that breaks carbohydrates (starch etc.) down into glucose. It facilitates glucose uptake from the blood. It is secreted with saliva into oral cavity, where it begins to break starch down, or with pancreatic juice into duodenum. Acid gastric juice inactivates amylase. The experiments have

shown that after 80 g glucose was administered, amylase administration ensured that blood sugar indices remained normal. 86% of patients with diabetes have a small amount of amylase in their intestinal secretion. Being an enzyme produced by pancreas, amylase level in the blood and urine rises sharply, in the progress of pancreatitis.

24. **Bilirubin** is a pigment, formed as a result of hemoglobin breakdown, and to a lesser extent as a result of megaglobin breakdown. The determination of total bilirubin and its fractions is very important for the differential diagnostics of jaundice of various etiology. The elevation of unconjugated bilirubin level in the blood and tissues is determined with hemolytic jaundice. In hepatocellular jaundice, hepatocytes are being destructed , conjugated bilirubin excretion into the bile capillaries is impaired and it leaks into blood, where its level elevates significantly. Moreover, ability of the hepatocytes to synthesize bilirubin-glucuronides reduces. Consequently, unconjugated bilirubin level elevates. In obstructive jaundice, the biliary excretion is impaired, which leads to steep elevation of conjugated bilirubin level.

27. The concentration of plasma protein. Plasma proteins are divided into three groups: albumins, globulins and fibrinogen. Being colloids, proteins bind and hold water, preventing its outflow from the bloodstream. Some plasma proteins, fibrinogen in particular, are basic components of blood clotting. Blood plasma proteins are one of the most important circulatory buffers, which support level of blood cations by forming nondialyzable compounds with them. The clinical prac-

tice has evidenced conditions, defined by the change of total plasma proteins. Hyperproteinemia is a increase of total protein concentration in the plasma. It is seen with diarrhea, vomiting, obstruction of the upper small intestine and water loss. Hypoproteinemia, i.e. a decrease in the total protein concentration, is seen in the patients with neurotic syndrome. In addition, it occurs with hepatocytic lesions, and with the disorder of renal filter (lipoid nephrosis). Generally, we may relate hyperproteinemia to hyperglobulinemia and hypoproteinemia to hypoalbuminemia.

Oxygen consumption and transportation:

28. **Plasma density**. The plasma density is defined by total amount of plasma cations and anions. 1048 - 1055 g/cm3 is a norm. Changes in the plasma density are attributed to the disorders of water metabolism. These processes are greatly effected by antidiuretic hormone. It can be seen with Conn's syndrome, which is associated with the changes in aldosterone level. When plasma density is lower 1056, this results in blood pressure instability, hypodynamia, sometimes convulsions.

29. **Circulatory blood volume**. The volume of circulatory blood is a genetic value and makes up 68-70 ml/kg for men and 65-69 ml/kg for women. The changes of these values are attributed to water and electrolyte imbalance, as well as to the diseases of intestinal tract and kidneys.

30. **The minute volume of circulatory blood**. This is a value resulting from the functional state of organ-

ism, and is connected with respiratory rate and heart rate. The average values, calculated for a person weighing 70 kg, are 4-4.5 ml/min.

31. **Oxygenation rate**. It is a rate of oxidative processes, taking place in erythrocyte and in the cells. This value is formed under the influence of lipid peroxidation, which defines permeability of cell membranes, composed of lipoprotein complexes. Also, this value is related to the state of liver, gastrointestinal tract, and kidneys. The oxygenation rate is affected significantly by the temporal relations of blood circulation in the systemic and pulmonary circulation.

32. **Surface of gaseous exchange**. It is a erythrocyte respiratory surface, which averages 350000 cm^2.-43000 cm^2. Value of the surface of gaseous exchange varies with the corpuscular volume, age, weight and sex.

33. **Vital lung capacity**. This is a value, representing lung ability to receive blood circulation minute volume, which defines alveolar surface area, participating in respiration.

34. **Transportation of oxygen**. It is a value, depending on the functional and morphological state of systemic and pulmonary circulation, and first of all on: lungs, heart, liver and gastrointestinal tract.

35. **Quantity of consumed oxygen per 100 gram brain tissue** is associated with a complex cause, involved in the redox processes, lipid peroxidation reactions, and with a state of thyroid blood circulation regu-

lation. Thyroid blood circulation determines the transportation of oxygen and its consumption by inner organs due to the activation of thyroid hormones T3 and T4. This index depends on the activation or inactivation of organ oxygen consumption. This value averages 2.5-3.5 ml/100 g tissue for adults and 3.5-6 ml/100 g tissue for children.

36. **Arterial blood oxygenation** is related to hemoglobin ability to bind oxygen and oxygenate tissues. To a great extent, this process is affected by thyroxin. Thyroxin splits oxidation and phosphorylation processes, reduces high energy phosphate bond formation and increases development of heat, which dissipates in the environment. Oxygenation curve is connected with atmospheric pressure, blood pressure and active site temperature.

37. **Cardiac output** is a part of minute volume of blood, being pumped by heart as a result of heartbeat. The cardiac output value is influenced by the intensity of myocardial contractions, pressure in the pulmonary circulation, de Ritis coefficient, aspartate transaminase activity, and regulation state of the creatinine-kinin system.

38. **Oxygen consumption per kilogram weight**. This dimension is attributed to the triiodothyronine activity. We can arrange organs, in descending order, in respect of triiodothyronine influence on the oxygen consumption per kilogram body weight as follows: heart (10-11%), gastric mucosa, liver, smooth muscles: 4-5%, kidneys (1%), diaphragm (4%).

39. **Pulmonary ventilation** is a correlation between entering air volume and exiting air volume per minute. The pulmonary ventilation average depends on sex, age and weight, and makes up 8 -10 l/min for a person weighing 70 kg.

40. O_2 consumption per minute is related with the state of pulmonary circulation, systemic circulation, liver, kidneys, and gastrointestinal tract. The triiodothyronine activity has primary meaning in the oxygen consumption per minute.

41. **Myocardial oxygen consumption** is a value, dependent on the functional state of organism. When myocardial oxygen consumption increases, stomach, liver and smooth muscles consume less oxygen, which predetermines activation of the enzymes, creatinine kinase in particular.

42. **Deficit of circulatory blood** is a depression in the circulating blood volume per kilogram body weight and circulatory minute volume expansion. Exposure to the deficit of circulatory blood is attributed to the processes, regulating water-salt metabolism. It is understood that watersalt metabolism is influenced by the thyroid hormones. Combined interactions between pituitary antidiuretic hormones, somatotropic hormone, and kallikrein-kinin system are accompanied with changes in the plasma density and urine specific gravity. As the difference between plasma specific gravity and urine specific gravity is decreasing, we observe drop in the colloid-oncotic pressure, resulting in the rise of capillary hydrostatic pressure. The changes in colloid-oncotic pressure and hydrostatic pressure

causes water outflow to the intercellular space and depression in the circulatory minute volume, and so rise of the deficit of circulatory blood.

43. **Vital lung capacity in an expiration phase** is a lung volume after expiration. The more the lung volume in the expiration phase, the more the pulmonary residual volume and the worse is the functional state of lungs.

44. **Maximum air flow** is an expiratory air speed. The reduction in air flow speed is of fundamental importance. The lower is the speed, the higher is pulmonary residual volume, i.e. there is decrease in the interrelations between alveolar volume and circulatory blood volume. Generally, decrease of the air flow is an evidence of the following diseases: bronchitis, pneumonias, lung neoplasms, abscesses.

45. **Tiffeneau's test** is a relation between time of the pulmonary circulation and time of the systemic circulation. Tiffeneau's test defines elasticity of the cardiorespiratory system. The less is Tiffeneau's test, the higher is a resistance of the pulmonary circulation. Decrease in the Tiffeneau's test is accompanied with increase in the minute pulmonary circulation and decrease in their alveolar surface.

46. **Fibrinogen**. It belongs to the acute phase plasma proteins and its level rises in all inflammatory and destructive processes. It participates in the blood-clotting system. Its increase is supplemented with the increase of y-globulins and hypoproteinemia.

47. **Creatinine concentration**. As to the nature of formation, we distinguish between exogenous and endogenous creatine. Endogenous creatine is formed in the process of tissue synthesis. Mainly, creatine synthesis occurs in the liver, wherefrom it is transported to muscular tissue via bloodstream. Here, creatine adds phosphorous group and turns into creatine phosphate, and then the latter forms creatinine . The following amino acids participate in the creatine synthesis: arginine, glycine and methionine. Such diseases as myasthenia, myatony and myositis are accompanied with abnormal processes of creatine transformation to creatinine. Rise of the creatinine level in serum is seen with kidney diseases. Constant rise of the creatinine level is indicative of the disorders of renal filter. Doubling of blood creatinine is parallel to the decrease in renal filtration by 50%.

48. **Dopamine β-hydrolase**. It is an enzyme, found dissolved in lysosomes. Dopamine β-hydrolase activity is attributed to pH optimum. If pH in the functioning cell is normal, free amino groups of hydrolases in lysosomes form the ionic bonds with acid phosphate groups of lipoprotein lysosomal matrix. These ionic bonds determine hydrolase latency inside lysosomes. Destructive processes in the tissue are connected with the pH changes and activity of lysosomal hydrolases. The idea is that their activity changes type of the cell membrane construction. Dopamine β- hydroxylase level decrease is accompanied with the development of various asthenodepressive and asthenoneurotic states.

49. **Lactic acid**. It is a final product of glycolysis and glycogenolysis. The lactic acid concentration is related with status of the blood circulation in muscles and liver. It increases with muscular activity. Rise of the lactic acid concentration can be seen with hypoxia (cardiac, pulmonary insufficiency), anaemias, neoplasms, acute hepatitis, terminal hepatocirrhosis, toxicoses. Thus, increase in the lactic acid concentration in blood is attributed to increase of its production in the muscles, and to the decreased ability of liver to transform it to glucose and glycogen.

50. **Urea**. All parts of residual nitrogen represent final products of protein metabolism. Concurrently, the main final product of protein metabolism is a urea. Ammonia is the primary source of urea formation. Urea level shifts depend on the process of urea formation and its excretion. These processes are interconnected with metabolism of amino acids (arginine and glutamine). The level of blood urea is decreased in hepatocirrhoses, acute yellow atrophy, phosphorous, arsenical and other poisoning, affecting liver. In general, increase of the urea concentration is accompanied with increase of creatinine and filtration reduction.

51. **Glucose** is the most important blood component. Its concentration reflects status of carbohydrate metabolism. Glucose is distributed, almost equally, between plasma and formed elements of blood. Blood sugar concentration changes with age. Sugar concentration in newborns is the same as sugar concentration in their mothers. After birth, sugar concentration is decreased rapidly and makes up 65 +-30 mg/%. By the age of 5-6 days, glucose concentration reaches 75+-

20 mg/% (by the Hagedorn-Jensen method). The level of glucose is regulated by central nervous system. Exogenous glucose is processed in the digestive tract and transported to the liver. Amino acids, glycerin, and lactic acid participate in the glucose formation. Sequence of the glucose formation processes ensures glycogenesis, resulting in the formation of liver glycogen. Later on, liver glycogen undergoes changes in the so called glucose blood pool: glycolysis, glycogenesis, and aerobic decomposition, resulting in the formation of CO2 и H_2O. Lipogenesis, supporting lipid synthesis in the tissues, biosynthesis of the substituted acids and protein synthesis. The changes in sugar level may be considered as a result of excitation of the metabolic centers by pulses of the energy-starved chemoreceptor cells. The liver ensures maintenance of the constant blood sugar level. Its spare capacities in this regard are ensured by the interaction of somatotropic hormone, insulin and glucogon. Synchronism in working of this system is ensured by the regulation of glucose consumption through lipid oxidation and enhanced intake of glucose in the intestine with the help of thyrotrophic hormones, thyroxin, and adrenocorticotropin.

52. **Triglycerides (TG)** belong to the energetic substrates. TG are important constituent of food, used to recover metabolic consumed energy. An adult organism receives 60-80 g fats (TG), 85% of which being split in the gastrointestinal tract (pH~5). TG splitting in the stomach leads to the formation of free fatty acids, which are released to the intestine, where, under the influence of steapsin, fatty acids (TG) split to monoglycerides. This process is regulated by entero-

statin ("gastrointestinal hormone"), initiating a sensation of fullness during food intake and digestion.

Fatty acid oxidation:

53. **Cholesterol**. Conditionally, we can distinguish three cholesterol pools in a human organism: pool A – rapidly exchanging (ca. 30 g FC (free cholesterol)), pool B - slowly exchanging (ca. 500 g FC) and very slowly exchanging (ca. 50 g FC). Experimental data showed that 6 mg cholesterol accounts for 1 g body weight. Major portion of nonestherificated cholesterol (NEFC) occurs in cell membranes and myelin sheathes, containing phospholipids. In plasma membrane, molar correlation of NEFC with phospholipids is equal to 1. Cholesterol synthesis occurs in almost all cells and tissues, however it is produced considerably in the liver – 80%, and in the small intestine walls – 5%. As a first approximation, cholesterol biosynthesis can be divided into three stages:

1. Mevalonic acid biosynthesis.
2. Squalen formation from mevalonic acid.
3. Squalen cyclization and cholesterol formation.

The main source of mevalonic acid formation in the liver is acetyl coenzyme A, and in the muscular tissue, it is lycine. Cholesterol oxidation to bile acids in the liver hepatocytes is main way of the metabolic elimination of this hydrophobic compound from organism, and bile acids themselves can be considered as a final product of the cholesterol catabolism. In addition, great role is played by taurocholic and glycocholic acids, which are involved in the pH regulation. The enzymes

of large intestine microflora affect formation of the sterols, not containing carboxylic groups.

54,55. Lipoproteins. Lipoproteins, rich in triglycerides – chylomicrons (CM), and very low-density lipoproteins (VLDLP). CM are formed in the process of edible fat absorption and serve to transport exogenous TG to the sites of utilization (cardiac and skeletal muscles, mammary glands etc.) and depositing (adipose tissue). Apoproteins of all major groups are found in the CM protein part.

56. **VLDLP**. They represent a transport form of the endogenous TG. The protein concentration in VLDLP is higher than in CM. Lipid and protein compositions of VLDLP are subject to the significant quantitative changes more, than in any other LP class. Main proteins of VLDLP are apo B-100 and apoproteins of C group. Usually, VLDLP lipids are isotropic liquids, and they are adequately mobile, which is identified by the constant lateral moving inside one particle and between particles. Practically, all TG in the nucleus of LP-particle are liquid at 37°C . VLDLP are formed in the liver, in endoplasmic reticulum ribosomes of hepatocytes. Latest data showed that VLDLP assembly is greatly influenced by microsomal TG-carrying protein.

57. In bloodstream, **CM and VLDLP** make contact with the lipid components of membranes of red cells, weight cells, endotheliocytes and other cells. These contacts are exposed to the lipolytic enzymes. This exposure leads to the delipidization and partial deproteinization. It is illustratory, that, after being formed, remnant particles of CM and VLDLP continue enrich-

ing itself in apo-E through its transition from VLDLP. 58. Rich in cholesterol VLDLP. Protein component is presented by apoproteins B, C, E. Approximately ¾ of total protein of these LP accounts for apo-B. In a certain manner, molecular and immunochemical heterogeneity of VLDLP is connected with atherogenesis and can serve as a additional criterion of its evaluation.

Carbon dioxide transportation and consumption:

59. **CO_2** release is indissolubly related to the oxygen consumption and CO_2 generation in organism. CO_2 is generated in organism as a result of biochemical transformations of glucose, amino acids, fats in the liver and blood under the influence of enzymes. Since glucose is one of the main oxygen source for a cell, its level is connected with CO_2 generation and release in organism. Under the influence of glucose oxydase, glucose is oxidized by air oxygen to gluconic acid, and hydrogen peroxide in equimolecular quantities is formed. In this relation, CO_2 generation rate must be lower than CO^2 release rate, and total venous blood CO_2 must be higher than total arterial blood CO_2.

62. **CO_2 generation rate** is a biochemical process, related to metabolism and oxygen consumption by organism. CO_2 generation rate is greatly influenced by pH environment and lactate indices.

63-69. **Internal organ bloodstream in ratio to general bloodstream**. Whole bloodstream (MCV), taken for 100%, is distributed among organs. Average data are taken from V.P. Osipov's monograph “Principles of Cardiopulmonary Bypass” (1976); V.A> Berezovskiy's

"Oxygen Tension in Human and Animal Tissues" (1975), C. Caro's "The Mechanics of the Circulation" (translated from English) (1981), V.P. Parins's "The Physiology of Circulation". Important indices are cardiac and cerebral blood flow. When cardiac blood flow decreases below 4%, various variants of cardiac circulatory insufficiencies are observed. When cerebral blood flow decreases below 13%, various clinical variants of cerebral circulatory disorders can be seen.

70-76. **Internal organ bloodstream in ml/min**. Bloodstream of inner organs in percentage terms was recalculated as to the general blood flow in ml/min. The data used were the same, as taken from V.P. Osipov's monograph "Principles of cardiopulmonary bypass" (1976); V.A> Berezovskiy's "Oxygen tension in human and animal tissues" (1975), C. Caro's "The Mechanics of the Circulation" (translated from English) (1981), V.P. Parins's "The Physiology of Circulation". In assessing the bloodstream of inner organs, it is necessary to analyze level of the myocardial and cerebral oxygen consumption.

77. **Acetylcholine**. As to Pokrovskiy's data, there are more than 100 methods of chemical cholinicity determination in various blood activities. Choline esterase activity is attributed to acetylcholine with pH environment value. pH value has an impact on delivery of acetic acid, and this reactions continues until environment pH achiebed defined level. Choline esterase activity varies widely. Distinctive decrease of choline esterase is seen with hepatic diseases, hypothyroidism, bronchial asthma, and rheumatoid arthritis.

79-81. **Cardiomechanics intervals**. Cardiac beat cycle begins in certain area, in the right atrium wall, called “pacemaker”. Muscle cells in this area are specific: they are able to polarize and re-polarize from time to time. Having begun in the pacemaker, depolarization travels, at a speed of 1 m/s, to neighboring walls of right and left atriums, causing their contractions. Then, depolarization acts on muscle bundle (His band), which passes through fibrous tissue, surrounding tricuspid valve, to interventricular septum. Depolarization wave is quickly propagated in this pathway at a speed 5 m/s. Ventricular depolarization potential on ECG (QRS complex) lasts less than 0.1 s. Depolarization and repolarization cycles generate weak electric potentials. Atrial depolarization results in small deviation, called P wave, 0.2 s delayed. This wave is followed by the sharper potential oscillation, known as QRS complex. It reflects the depolarization of both ventricles. After that, another component, T wave, appears. Temporal relations between these total mechanic events are accompanied with the changes of pressure in left atrium, left ventricle and aorta, as well as blood flow in aorta during full cardiac cycle.

82. **Left ventricle contractions**. In ECG, beginning of the left ventricle contraction is signalized by QRS complex. At very short interval, after depolarization, muscle fibers, ventricular walls begin developing active tension, where contractile elements of myocardial cells, known as myofibrils, participate. Myofibrils consist of bundles of filaments, which, in turn, form repeating chains, sarcomeres. Because of their contraction, pressure in the left ventricle starts rising. At this stage, aortic valve is still closed, since aortic pressure higher

than pressure in the left ventricles, and mitral valves come closer as the blood flow from atrium to ventricle decreases. This status is of short duration, since ventricular pressure promptly exceeds atrial pressure. This periods ends with mitral valve closure. Ventricular wall tension starts growing very fast, and continues growing until ventricular pressure exceeds aortal pressure. Once ventricular pressure is higher than aortal one, a system of forces occurs, which opens aortal valve. Blood percentage, driven out of the heart during blood expulsion, is characterized by the left ventricle contraction capacity. Cardiac output is a part of minute volume of blood, being pumped by heart as a result of heartbeat. The cardiac output value is influenced by the intensity of myocardial contractions, pressure in the pulmonary circulation, de Ritis coefficient, aspartate transaminase activity, and triiodothyronine and tetraiodothyronine activity.

83,84. Arterial pressure. Speaking of blood pressure, we always mean pressure, measured relative to the atmospheric pressure. Usually, it is taken that pressure in the body tissues directly near outer arterial walls is equal to the atmospheric pressure, so blood pressure is considered as transmural pressure (transmural pressure represents difference between inner (ip) and outer (op) pressures, where ip is a pressure inside artery, and op is an outer pressure, equal to the atmospheric pressure). Arterial pressure generation is controlled by rennin-angiotensin system and kinins (bradykinin), hormones of adrenal zona glomerulosa layer, participating in the regulation of sodium and potassium electrolyte metabolism. The main hormone, regulating mineral sodium and potassium metabolism,

is aldosterone. In addition, arterial pressure generation is influenced by hormones of adrenal medulla (adrenalin, noradrenalin and dopamine), which regulate cardiac tone and lumen.

85. **Pressure in pulmonary circulation**. Pulmonary circulation is a low-pressure system: in a healthy man. Average pressure (i.e. pressure over the atmospheric one) in the right ventricle and in major pulmonary arteries makes up approx. 15 mm Hg or 130-140 mm CE. Issue of the pressure generation is connected with blood volume, flowing in the vessels of pulmonary circulation. In healthy man, this value makes up 0.5 l or 10% of circulating blood volume. Veins of pulmonary circulation contain nearly half of blood volume, flowing in the pulmonary circulation. Healthy test subjects showed increase in the oxygen consumption during muscle work. Pulmonary artery pressure rose, on the average, from 13.9 mm Hg to 17.3 mm Hg. Blood volume in the pulmonary circulation capillaries is influenced by lung volume, defined as a ratio between 30 and 33 indices.

86. In norm, **width of third ventricle** is 4.5 – 6 mm. The size of third ventricle is greatly influenced by a number of factors, participating in the regulation and distribution of water metabolism in the body. We can distinguish 5 factors, which define the flow of body liquids between various spaces:

1. Osmotic pressure, related to the difference between concentrations of substances, dissolved in liquids, which are separated by semiimpermeable membrane.

2. Factor, influencing the flow of liquids, i.e. hydrostatic pressure, occurring in lumen being subject to the heart force. The balance between hydrostatic, hydrodynamic and oncotic pressures defines the flow of liquids from vessels to tissues and visa versa.

3. Permeability of cell and vascular walls, and other membranes. It is connected with certain biochemical processes.

4. Active biological mechanism of ion migration, The systems of active transport maintain transport of substances against their concentration gradient with the consumption of macroergic phosphate energy.

5. Active regulatory mechanisms, which define the level of water and sodium loss in such nodes, as the points of contacts between internal and external environment of the organism. First of all, these are renal regulating mechanism, pituitary antidiuretic hormone and aldosterone.

89. **Systemic circulation time** is a time of a full and complete cycle of blood flow through the systemic circle vessels, related to five factors of the regulation of blood circulation in inner organs. These factors are indissolubly related to the regulation of water-electrolytic metabolism.

91. **Spectral wavelength of CO_2 absorption in the blood**. This index characterizes hypocapnia and hypercapnia.

92. **Spectral wavelength of N_2O absorption**. This index characterizes nitrogen metabolism in the body. When it is lowered, the destructive processes can be often observed. When assessing this index, it is nec-

essary to analyze blood circulation in the inner organs and creatinine kinase activity. Special attention need to be paid to the medical history taking.

93. **H_2 concentration in gastric juice**. The number of hydrogen protons is related to the whole complex of biochemical transformations. First of all, they are related to the interactions between gastrointestinal hormones (GIH), glucagon, vasoactive intestinal polypeptide (VIP), and gastroinhibiting intestinal polypeptide. The interaction of these hormones defines active sodium participation, the latter being main plasma cation, influencing venous pressure. Rise in venous blood pressure causes hydrostatic pressure to increase. When hydrostatic pressure is higher than oncotic pressure, this can cause electrolytes out of intercellular space. This phenomenon leads to hypovolemia and activation of the juxtaglomerular apparatus of kidneys. This results in stimulation of the adrenal cortex and increase in aldosterone secretion. In a whole, these factor combinations give rise to the changes in pH environment and organotrophic disorder.

94. **Blood pH** is a concentration of hydrogen protons, participating in the tissue respiration, under which mitochondria supply required energy, in the form of macroergic phosphates. it is necessary to supply oxygen and to release carbon dioxide. The oxygen is supplied to the cell with blood flow, likewise carbon dioxide is released from the cell. Blood is a part of body internal environment with well-defined concentration of the transported substances. Hydrogen ion concentration is a very important constant, defining full value of the metabolic transformation in cell, which determines

body need in working systems aimed at supporting constant hydrogen ion concentration by the excretion of redundant hydrogen ions or their retention in case of deficit. This mechanism is supported by buffer systems. The most powerful blood buffer is proteins, hemoglobin in particular. Hydrogen ion concentration is regulated by bicarbonate buffer, consisting of carbon dioxide and sodium bicarbonate. Another buffer is a phosphate one. Mono-substituted phosphate serves as an acid, and twice-substituted phosphate serves as a salt. Phosphate buffer is closely related to bicarbonate and protein buffer systems, with kidneys supporting decrease or increase of bicarbonate level when pH changes. The main mechanism of supporting concentration of hydrogen ions, represented in renal tubule cells, is a process of sodium reabsorption and hydrogen ion secretion.

97. **Glutamic acid** is an amino acid, which regulates metabolic processes and affects ion concentration (sodium, potassium etc.). Required sodium ion concentration in the body is supported by formation of ammonia in the kidneys and its use for neutralizing acid equivalents and their renal excretion. Resulting free ammonia easily penetrates into renal tubular lumen, where being combined with hydrogen ion, it turns into poorly diffusing ammonia ion. In the conditions, accompanied with glutamic acid deficit, compensatory mechanisms are not able to prevent shifts in the hydrogen ion concentration, which leads to the acid-base imbalance. The reasons can be as follows: decrease of respiratory minute volume, circulatory inefficiency, pulmonary sarcoidosis, rheumatoid arthritis, acute

pneumonia. All these pathological states are accompanied with glutamic acid deficit.

98. **Tyrosine acid** is a regulatory amino acid, being constituent of the thyroid hormones. Thyroxin and triiodothyronine are iodated tyrosine derivatives.. Blood iodine is captured by thyroid tissue by means of the active concentration mechanism. In the thyroidal tissue, iodine is peroxidase oxidized to form monoiodtyrosine. As a result of tyrosine iodination in fifth residue, diiodtyrosyne is formed. Monoiodtyrosine conmination results in triiodothyronine (T3). Complexation of two diiodtyrosyne molecules leads to the thyroxin formation (T4). Thyroid hormones are of significant importance for the processes of growth, development and pubescence. They raise energy consumption in tissues, protein synthesis and glycometabolism, and affect lipid metabolism.

99. **Creatinine kinase in muscles**. Creatinine kinase catalyzes reverse reaction of phosphoryl residue transport from ATP to creatine from creatinine phosphate to ADP. Creatinine phosphokinase acts in a dual manner in the muscular tissue: in sarcoplasm, enzyme transports phosphoryl group from ATP to creatine; resulting creatinine phosphate is used for phosphorylirazing ADP, which is combined with myosin in myofibrils. This system, along with sodium and potassium and stimulated ATPase, participates in energy supply to the active ion transportation through cell membranes.

100. **Creatinine kinase in heart** is divided in three types:

1. Isoenzyme 1-BB (characterized by high mobility, attributed to the temperature changes, mainly in the abdominal region).
2. Isoenzyme 111-MM (moves at a lower speed)
3. Isoenzyme 11-MB (in-between position as to mobility).

Heart contains mainly MM and MB forms. It is assumed that energy of the transport from mitochondrion to cytoplasm of myocardial cell is transferred through the internal mitochondrial membrane. In intermembranous space (Mg2+ occurrence), a balance is being established between ATP - Mg2+ and CFK*ATP - Mg2+ complex at the outer side of internal membrane. A considerable increase of CFK is seen with musculoskeletal disorder and in acute myocardial infarction. Thus, CFK activity increases earlier than activity of other enzymes. High CFK activity is observed in various central nervous system diseases: schizophrenia, manic-depressive psychosis, syndromes, induced by psychotropic agents.

101. **Glycogen** is a reserve energetic substrate. Conditions for accumulation of some reserve carbohydrates are created due to its ability to deposit in the liver and muscles. When energy consumption increases, glycogen usually decomposes. Thus, this process is accompanied with the increase of function of some endocrine glands (thyroid, adrenal medulla, hypophysis), secreting hormones, which activate glycogen decomposition. Due to glucose formation, glucocorticoids prevent hepatic glycogen from being destroyed. Thyroid hormone, thyroxin, facilitates glucose

absorption in the intestine. Blood glycogen concentration increases in hepatolienal syndromes, diabetes, malignant growths. Hereditary diseases with glycogen metabolism disorders hold a special position.

102. **Used power of life support**. Average power, used for life support, is 2300 kcal per 24 hours for man, weighing 70 kg. Used power of life support is ensured by the changes of free energy with complete combustion of 1 mole palmitic acid making up 2338 kcal. High-energy phosphate bond is characterized by value 7.6 kcal/mole. Thus, with total oxidation of one palmitic acid molecule, it makes up 130 ATP molecules. Being recalculated to kilogram, this value changes from 1 to 20 kcal/kg/min and more. It is related to arterial blood oxygenation and hemoglobin ability to bind oxygen and oxygenate tissues. To a great extent, this process is affected by thyroxin. Thyroxin splits oxidation and phosphorylation processes, reduces high energy phosphate bond formation and increases development of heat, which dissipates in the environment. Thus, oxygen consumption changes to kg. This dimension is attributed to the triiodothyronine activity. We can arrange organs, in descending order, in respect of triiodothyronine influence on the oxygen consumption as follows: heart, gastric mucosa, liver, smooth muscles, kidneys, and diaphragm.

103. **Working level of oxygen consumption**. It is related to arterial blood oxygenation and hemoglobin ability to bind oxygen and oxygenate tissues. To a great extent, this process is affected by thyroxin. Thyroxin splits oxidation and phosphorylation processes, reduces high energy phosphate bond formation and

increases development of heat, which dissipates in the environment. Thus, oxygen consumption changes to kg. This dimension is attributed to the triiodothyronine activity. We can arrange organs, in descending order, in respect of triiodothyronine influence on the oxygen consumption as follows: heart, gastric mucosa, liver, smooth muscles, kidneys, and diaphragm, i.e. with triiodothyronine activity increasing, activity of the oxygen consumption by heart and other inner organs increases as well. If oxygen consumption by heart increases, oxygen consumption by gastric mucosa, liver and diaphragm changes (decreases) as well. This results in the deficit of used power for life support.

104. **One-time load time**. We mean physical activity, done by man, taking into account kcal consumption and their recovery in a certain period of time. It is connected with energy storage efficiency due to the fatty acid oxidation, and makes up 40%, which is close to relevant glycolysis, tricarboxylic acid cycle and oxidative phosphorylation. One of the fatty acid oxidation products is hydrogen peroxide, with active electrons transported directly to oxygen. This reaction is related to hemoglobin ability to bind oxygen and oxygenate tissues. To a great extent, this process is affected by thyroxin. Thyroxin splits oxidation and phosphorylation processes, reduces high energy phosphate bond formation and increases development of heat, which dissipates in the environment. Thus, oxygen consumption changes per body weight unit. Thus, one-time load time will depend on the splitting of fatty acids, being of chain nature and connected with the blood circulation in inner organs.

105. **Respiratory coefficient** is defined by the interaction between oxidative processes and processes, involved in lipid peroxidation. Great importance is attached to the platelet-activating factor, which leads to the aggregation of these cells, with serotonin being released. The latter is a vasoconstrictive agent and a stimulator of unstriated muscle contractions. In this connection, platelet-activating factor affects white blood cells, thus stimulating chemotaxis, degranulation and aggregation of polymorphonuclear leukocytes with them producing superactive radicals. Platelet-activating factor represents a phospholipid bioregulator and is associated with lipoproteins and high-density lipoproteins. Thus, respiratory coefficient is determined by a combination of biochemical processes, set forth in clauses 102-103 above.

106. **Tyrosine**. Thyroid hormones, thyroxin and triiodothyronine, are iodated tyrosine derivatives. Tyrosine is present in food and in the body in high volume. Due to the influence of pituitary thyrotrophic hormone on thyroid, proteolytic enzyme are activated, which release thyroxin and triiodothyronine form the bond with thyreoglobulin molecules. The primary points of thyroxin application in tissues are cytomembranes, nuclei, and enzymes of the biological oxidation system. Thyroxin increases generation of heat, which dissipates in the environment. Triiodothyronine increases oxygen consumption by the tissues, heart in particular. Concurrently, there is a change in heat generation degree, which is defined by catecholamine deficiency.

107. **Cerebral blood flow**. Regulation of the cerebral blood flow per 100 g tissue is determined by the interaction of extra- and intracranial factors. Among extracranial factors are atmospheric pressure, gas composition of air, partial gas pressure in the atmosphere, wavelength of Xe86. These factors affect chemoreceptors, baroreceptors, photoreceptors, pressure receptors, thus ensuring sufficient cerebral blood flow per 100 g tissue. It is understood that one of important indices of cerebral blood flow is a width of third ventricle. Normally, it is 4.5 – 6 mm. The size of third ventricle is greatly influenced by a number of factors, involved in the regulation and distribution of water metabolism in the body. Adrenal medulla hormones, adrenalin, noradrenalin and dopamine, are of significant importance. They can be treated as successive links of amino acid, phenylalanine and tyrosine transformations. Due to the influence of pituitary thyrotrophic hormone on thyroid, proteolytic enzyme are activated, which release thyroxin and triiodothyronine form the bond with thyreoglobulin molecules. The primary points of thyroxin application in tissues are cytomembranes, nuclei, and enzymes of the biological oxidation system. Thyroxin increases generation of heat, which dissipates in the environment. Triiodothyronine increases oxygen consumption by the tissues, heart in particular. Concurrently, there is a change in heat generation degree, which is defined by catecholamine deficiency. Generally, catecholamines are considered to be humoral regulatory agents of sympathoadrenal system. The biological effect of the latter is the release of energy (stimulation of glycogenolysis, lipolysis, oxidative processes). Catecholamines activate nervous system, changing heart rate, and increase peripheral

circulation in some vascular regions. The combination of these effects exercises a mobilizing and regulatory influence on human organism, vegetometabolically ensuring body adjustment to conations by changing the blood flow in inner organs and optimizing cerebral blood flow.

108. **Testosterone** belongs to sex steroids, which influence secondary sexual characters development, pubescence, and sexual function.

109. **Estrogen** belongs to sex steroids, which influence secondary sexual characters development. Functional activity of these hormones is realized through hypothalamic factors, somatotropic hormone secretion in particular. Its structure reminds of prolactin and placental hormone chorionic somatomammotrophin, which defines closeness of the biological activity. In this relation, testosterone, estrogens and thyroxin stimulate somatotropic hormone secretion, and with hypercorticonemia, they suppress it.

110,111,112. **Water-salt metabolism, water distribution in the body**. Water, among other components of human body, plays the most important role, being solvent both for organic and nonorganic substances, and represents a base for body internal environment. Most part of water is included as a compound to intracellular fluids. Extracellular water, in its turn, is a part of intercellular and intravascular fluids. As to Bland's data, water distribution in a body, in percentage from body weight and in absolute values, makes up: total body water in women 44-60%, or 38.5 l, in men - 50-70%, or 42 l. Intercellular water: women - 30-45%, or

28.5 l. Men - 35-50%, or 31.5 l. Extracellular water: women - 14-22%, or 9.8 l. Men - 15-22%, or 10.5 l. Intracellular water: women - 10-15%, or 7 l. Men - 10-18%, or 7.4 l. Plasma: for women – 4-5%, or 2.8 l. Men - 3.5-4.5%, or 3.2 l.

113,114. **Blood flow per 1 gr.of brain tissue and blood flow per 1 gr.of thyroid gland** ensures metabolism and energy consumption through water distribution in the body: metabolic free fraction and fraction, bound in the colloid systems with the molecules of organic substances. Per 1 g glycogen and protein, deposited in the tissues, 1.5 and 3 ml water are held respectively. As a result of catabolism in human body, 300-400 ml water is produced daily. Quantity of water determines the nature of decomposing substrates. With 100 g fat being oxidized, 107 ml water is produced, with 100 g protein – 41 ml water, with 100 carbohydrates – 55 ml water. All body water is renewed in 4 weeks. Whole system of the metabolism regulation is determined by the blood flow per 1 f brain tissue and blood flow per 1 g thyroid gland.

115. **Tissue oxygen extraction index** is interrelated to the cell membrane permeability, where cholesterol and phospholipids are of great importance. By hypothesis for the nature of bonds, involved in the interaction of phospholipids polar sites and cholesterol, cholesterol hydroxyl and ethereal oxygen become hydrogen bonded. At a phase transition temperature, phospholipids pass from a solid gel to a liquidcrystal state. Molecular nature of phase transition is attributed to the changes of average speed of oxygen supply, depending in the temperature. In special literature,

when assessing cholesterol role in the membrane structure and function it is considered that cholesterol facilitates decrease in mobility of fatty acid chains at high temperatures and increase in mobility at low temperatures.

116. **Oddi's sphincter basal pressure** determines hemodynamic effect, ensuring resynthesis of the intestinal wall lipids. According to the present-day ideas, triglyceride resynthesis occurs in the epithelial cells of small intestine villi. Triglycerides are the most high-calorie substances. At their complete oxidation, energy output makes up 9.5 kcal. Quantity of energy, stored in 1 g such free-of-liquid fat, as triglycerides, is six times as large as quantity of energy, stored in 1 g glycogen. In other words, if calories were deposited in human body in the form of glycogens, than in order to accumulate 128000 kcal one may rather need 13.5 g triglycerides than 80 kg glycogens. It is Oddi's sphincter basal pressure that provides daily caloric requirement of man through switching and regulation of fat and carbohydrate metabolism.

117. **Prothrombin index** is connected with platelet-activating factor. The latter belongs to the lipid bioregulators. Their action is based on the platelet activation with serotonin being released. The latter is a vasoconstrictive agent and a stimulator of unstriated muscle contractions. Conditions for thrombosis are provided due to the platelet aggregation and arteriostenosis. In this regard, main biological mechanisms are chemotaxis stimulation, olymorphonuclear leukocytes aggregation with the latter producing superoxide radicals.

27. Certificate

EC Certificate – Production Quality Assurance
Directive 93/42/EEC on Medical devices, Annex V

ORKI certifies that the manufacturer *Number of certificate:* **5-515-500-0706**

Research and Production Complex "Biopromin" Ltd.
30"a" Selyanska Str, atp.32, Kharkiv, 61157, Ukraine
50 Khalturina Str, apt.2, Kharkiv, 61038, Ukraine

with authorized representative in EU

Inter-Kep Ltd.
Kerepesi út. 15.
Budapest, Hungary

for the products

Noninvasive hemogram analyzer (AMP)

applies a quality system in the manufacturing process which ensures that the products are manufactured in conformity with the technical documentation (referred to in Annex VII and kept by the manufacturer)

Number of the audit report on the assessment: **TI-42/075/2007**

Provided the yearly surveillance is carried out successfully this certificate is valid until:

2012-06-20

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Egészségügyi Minőségfejlesztési és Kórháztechnikai Intézet
Institute for Medical Quality Improvement and Hospital Engineering

Előző név: Orvos- és Kórháztechnikai Intézet
Institute for Medical and hospital Engineering
Diós árok 3. H-1125 Budapest

Tel: +36 1 356 1522
Fax: +36 1 375 7253
Internet: www.orki.hu